WHY DOES THE U.S. DEPARTMENT OF VETERANS AFFAIRS CONTINUE TO GIVE A SUICIDE-INDUCING DRUG TO VETERANS WITH POST TRAUMATIC STRESS DISORDER?

HEARING

BEFORE THE

COMMITTEE ON VETERANS' AFFAIRS
U.S. HOUSE OF REPRESENTATIVES

ONE HUNDRED TENTH CONGRESS

SECOND SESSION

JULY 9, 2008

Serial No. 110–96

Printed for the use of the Committee on Veterans' Affairs

U.S. GOVERNMENT PRINTING OFFICE

43–998 WASHINGTON : 2009

For sale by the Superintendent of Documents, U.S. Government Printing Office
Internet: bookstore.gpo.gov Phone: toll free (866) 512–1800; DC area (202) 512–1800
Fax: (202) 512–2104 Mail: Stop IDCC, Washington, DC 20402–0001

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WEDNESDAY, JULY 9, 2008

U.S. HOUSE OF REPRESENTATIVES,
COMMITTEE ON VETERANS' AFFAIRS,
Washington, DC.

The Committee met, pursuant to notice, at 10:05 a.m., in Room 334, Cannon House Office Building, Hon. Bob Filner [Chairman of the Committee] presiding.

Present: Representatives Filner, Brown of Florida, Snyder, Herseth Sandlin, Mitchell, Hall, Hare, Berkley, Salazar, Rodriguez, McNerney, Space, Walz, Cazayoux, Buyer, Stearns, Boozman, Lamborn, Buchanan, and Scalise.

OPENING STATEMENT OF CHAIRMAN FILNER

The CHAIRMAN. This meeting of the House Committee on Veterans' Affairs will come to order. And we have an important hearing today, but before we get started, we have a couple of housekeeping things that need to be done.

First, I ask unanimous consent that all Members may have five legislative days in which to revise and extend their remarks. Hearing no objection, so ordered.

We also have to consider a resolution to designate a new Democratic Subcommittee assignment to include our newest Member of the Committee, Don Cazayoux.

[The resolution appears on p. 119.]

The CHAIRMAN. Don, make sure we do it right, okay?

Don agreed to fill the vacancy on the Subcommittee on Health, which was made available when Mike Doyle resigned from the Committee. The Democratic Members of the Committee agreed to the assignment on June 17th, and now it is before the full Committee to approve the actions of the Democratic Caucus. The list of the Democratic Members of the Subcommittee on Health are in front of you, and I would ask for a motion to approve the resolution.

Mr. BUYER. I so move.

Ms. BERKLEY. I second it.

The CHAIRMAN. We want to buy in Mr. Buyer on this. Motion made by Mr. Buyer, seconded by Ms. Berkley. All those in favor, say aye.

Opposed?

The motion carries unanimously.

Mr. Cazayoux, we welcome you to the Subcommittee on Health. We are looking forward to your participation.

Mr. CAZAYOUX. Thank you.

The CHAIRMAN. And from talking to you, I know—as a representative of a rural area, there are a lot of problems with access and we intend to be looking at this as a Committee, and in the areas that you represent.

Mr. CAZAYOUX. Thank you, Mr. Chairman and Members, as well as Ranking Member Buyer and Subcommittee Chairman Michaud.

I'm honored to serve on this Subcommittee. Obviously, it is a Committee I believe is essential for helping secure benefits for those who have put their bodies on the line every day, and I'm honored to be able to serve and I'll work hard as a Member of this Subcommittee to ensure that the veterans of this country achieve and are assured of the benefits that they deserve.

But thank you so much.

The CHAIRMAN. Thank you, sir, and welcome to the Committee. The Subcommittee will probably be meeting this week.

We thank all the Members of the Committee, our witnesses and those of you who are here to watch the proceedings. Like many people in this country, I was appalled when *The Washington Times* published articles revealing that the U.S. Department of Veterans Affairs (VA) was, and continues to use, the drug Chantix® in Cooperative Studies Program (CSP) 519 that is smoking cessation treatment for veterans with post traumatic stress disorder (PTSD).

[*The Washington Times* articles appear on p. 119.]

The CHAIRMAN. Some veterans with PTSD, enrolled in the VA smoking cessation study were being, and continue to be, administered Chantix®. The drug did receive Food and Drug Administration (FDA) approval in May of 2006. However, on November 20, 2007, the FDA issued an early communication about an ongoing safety review of Chantix®. It revealed that FDA had received reports of "suicidal thoughts and aggressive and erratic behavior in patients who have taken Chantix®."

At this point, I believe a prudent course of action would have been for the VA to suspend the study and immediately notify all patients of the possible danger. The loss of any veteran to suicide is a tragedy. Since December 2007, this Committee has held two hearings regarding the issue of veteran suicide; and that is why I fail to understand why the VA did not react when the FDA issued the early communication concerning the dangerous side effects of Chantix®.

A few months later, in February of 2008, the FDA issued a Public Health Advisory stating, "Chantix® may cause worsening of current psychiatric illness, even if it is currently under control and may cause an old psychiatric illness to occur. Symptoms may include anxiety, nervousness, tension, depressed mood, unusual behaviors and thinking about or attempted suicide." According to the records, the VA waited until the end of February 2008, that is, a month later, to send the letter and new consent form to study participants to notify them of the dangers associated with Chantix®.

The letter informed patients that they may experience an increase in psychiatric symptoms such as anxiety, nervousness, ten-

sion, depression, as well as untoward changes in behavior. It failed to mention in that letter that Chantix® may lead to suicide ideation or attempted suicide. That fact was buried in a consent form, and we have to put this in the context of issues that we have had with the VA on statistics about suicide, of taking the issue seriously.

We had two hearings where there seemed to be an attempt to downplay the numbers, a real lack of speed in giving this Committee information that the VA had; and downplaying, in fact, the sense that if you have 1,000 suicide attempts per month of veterans in your care, something is wrong. That is the context in which we are viewing this particular situation.

Whatever warning was issued was too late for Mr. Elliott, an Army veteran of Operation Iraqi Freedom. In February, as he will soon tell us he suffered a psychotic episode that led to a confrontation with the police.

And, Mr. Elliott, I appreciate you being here today. I know it is not easy to talk about these things, and we appreciate your interest in helping other veterans as well as yourself.

As I said, there are a series of incidents that have given us concern about this. Suicides in Dallas, for example; e-mails suggesting that VA providers downgrade the diagnosis of PTSD to adjustment disorder, to an e-mail downplaying the epidemic of suicides in the VA. They have caused all of us on this Committee to question the VA's accountability measures and the Department's dedication to addressing the mental health needs of our returning servicemembers.

So we want to look at not only the exact procedures for handling human research subjects and determining whether they were followed in design and execution of this smoking cessation study and explore whether there was adequate oversight of the study. I'd like also to find out about VA's responsibility to respond to the FDA advisories and VA's decision to continue to use Chantix®, a suicide-inducing drug, on veterans with PTSD.

But I think in a larger sense we use this hearing today to ask the VA to take responsibility and to hold people accountable for the numerous issues that have been identified over the last few months. Both e-mails that have become public because of legal action—not because they were just given to us—were explained by the VA with the term they were "unfortunate." These were more than unfortunate; these involve life and death of the soldiers and veterans under our care.

The Texas e-mail said: "Given that we are having more and more compensation-seeking veterans, I'd like to suggest that you refrain from giving a diagnosis of PTSD straight up, consider adjustment disorder." Four patients committed suicide in Dallas, and the psychiatric ward was forced to close. We keep hearing these things time and time again, but do not see any action or any sense of responsibility. Talk is cheap, especially when it comes to the safety and well-being of our veterans.

We have seen a pattern in all of these. It is deny, deny, deny. And then, when caught and confronted, it is cover up, cover up, cover up, and then minimizing the importance of the issue or show-

ing that this particular veteran is merely an anomaly. No one is held accountable and the system goes on.

When questioned on this and in the various articles that have appeared, the VA immediately wants to defend the process that is being followed. This is not about the process. It is about the veteran. And the question really today is, when will the VA stop being the veteran's adversary in these processes and start being the veteran's advocate? We're talking about our veterans, our children. We want them defended.

I would recognize for an opening statement, Mr. Buyer.

[The prepared statement of Chairman Filner appears on p. 82.]

OPENING STATEMENT OF HON. STEVE BUYER

Mr. BUYER. Thank you, Mr. Chairman for yielding.

By way of opening, I'd like for you to know I'm very bothered by the title of the hearing. You've titled this hearing "Why Does the VA Continue to Give a Suicide-Inducing Drug to Veterans With PTSD?"

Now, calling an FDA-approved drug, Chantix®, a suicide-inducing drug, I believe, is inflammatory and it is misleading. And I believe by titling this hearing as you have done misses the mark. The issue I believe before us on which we should focus is Human Subject Research Protection and whether the protocols of the Common Rule have been followed by the VA.

Now, at the end of your opening, I agree with you; when you then finally began to focus that we really need to look at the execution of procedures, I agree. And the response to these advisory opinions that come out of the FDA—in other words, how does the VA respond, what is the VA's response to these advisory opinions and how is it followed through, and focus on accountability and responsibility, I agree with you and join on that.

With the possible exceptions of Drs. Boozman and Snyder, I doubt that anyone on this Committee, including myself, has the expertise to determine which drugs should be used by the VA and what drugs should be placed on a formulary. We defer to the experts on these matters. And Chantix® is an FDA-approved drug since May of 2006, and it is used by over 7 million people worldwide to help them stop smoking.

Again, what I think the Committee should investigate is whether the veterans who volunteered to be research subjects were treated properly. The VA Office of Inspector General (OIG) briefed our Committee staff prior to this hearing, and we know what their preliminary findings are.

I'm very disappointed that long-standing problems with the VA research program have apparently not been corrected. Those problems relate to strict human research subject protections that require fully informed consent of patients before they participate in any research study. It appears VA may have failed to disclose important facts veterans need to make informed decisions before participating in these studies. If they were not provided full information about the possible risks for their involvement in the VA smoking cessation study, this is a major problem, one that is made worse because this would not be the first time that the VA has

found themselves in this position on not giving proper informed consent in VA research.

During the 108th Congress, while serving here as Chairman of the Oversight and Investigations Subcommittee, I introduced H.R. 1585 to establish the Office of Research Oversight within the Department of Veterans Affairs. The language of this bill became law, Public Law 108–170. The provisions of this law established within the Veterans Health Administration (VHA) an Office of Research and Oversight to monitor, review, and investigate matters of medical research compliance and assurance in the VA, including matters relating to the protection and safety of human subjects and VA employees participating in VA medical research programs.

Now, Mr. Chairman, I recall, when the Committee passed this, the VA fought us on this. So with your opening about you're challenged by the VA, not only did they fight us on this bill, we had also sought that this be an independent office, and they didn't want that at all. So we ended up having to compromise on some of the legislation.

What gave rise to the legislation was an OIG report entitled, "The Alleged Research Improprieties, Informed Consent Issues at the Jerry L. Pettis Memorial Veterans Affairs in Loma Linda, California," issued on October 7, 1999, along with several hearings that followed on VA research and informed consent issues.

The Committee then was briefed on potential research misconduct at the Albany VA in 2003, and we were informed by the VA Inspector General that the VHA was conducting an inquiry into the matter. We monitored that situation and there was an actual criminal prosecution from that. And so—the Committee, I think, took very appropriate action to create this office; so the purpose of the legislation was to avoid the occurrence of situations like the unfortunate one we are discussing here today.

So, Mr. Chairman, "In August 2003, the VA initiated a Cooperative Studies Program integrating practice guidelines for smoking cessation into mental healthcare for post traumatic stress disorder," end quote. This research project was to compare effectiveness of integrating smoking cessation with mental health treatment versus keeping them as separate treatment programs. The protocol medications for this research project included the nicotine patch and nicotine gum. In January 2007, the VA modified the protocol by adding Chantix®.

After FDA's approval of the drug for public use as of today, the VA has approximately 32,000 patients on Chantix®, and the Department of Defense has approximately 67,000 patients on Chantix®. On June 17, 2008, an article appeared in the front page of *The Washington Times* detailing the use of the drug, Chantix®, in the VA study and the subsequent effects that may have been caused by this drug in one veteran in particular. That same day, I wrote a letter to the VA, as well as the VA Inspector General, requesting an investigation and immediate briefing on the allegations detailed in *The Washington Times* article.

On June 18th, I, along with Committee staff and representatives from Congresswoman Brown-Waite's office, attended a briefing by the Principal Deputy Under Secretary for Health, the Chief of Research and Development, the Chief Officer of the Office of Research

and Oversight and the Acting Deputy Chief Research and Development Officer. At this briefing, we were provided a chronology of the events leading up to *The Washington Times* article.

The Committee staff again met with Dr. Kupersmith and Dr. O'Leary on June 19th and requested documentation of all amended informed consent forms for all study subjects, as well as all adverse drug reactions and serious adverse events related to this study that have been reported to VA's Cooperative Study Center in Albuquerque, New Mexico.

To date, neither the Committee staff nor I have seen the amended consent forms. I ask the Secretary to be prepared to explain the absence of these forms during the question-and-answer period during the testimony here today.

Because of the preliminary findings, on July 3, 2008, I further requested a nationwide investigation by the Office of Inspector General on human research subject protections. I will have much more to say about this when Dr. Daigh of the Inspector General's Office testifies.

The FDA and Pfizer are going to be testifying to inform the Committee about Chantix®. They are the only witnesses here today that can be considered experts or authorities on drug safety and Chantix®. I caution my colleagues that this Committee lacks the expertise, as well as the jurisdiction over the FDA and drug safety. This is a topic more appropriately addressed by the Committee on Energy and Commerce.

To attack a legal drug as being unsafe and to characterize it as suicide-inducing, I believe is irresponsible and inflammatory. We should be careful in making sensational public statements about the safety of an FDA-regulated drug without full information about such drug when it could be also an enormous benefit in saving lives in the cessation of smoking.

There are many, many drugs, and we all take some of these drugs that have tremendous side effects. For example, there is a drug that all of us take every day, Mr. Chairman. It is called aspirin. One of the side effects of aspirin is anticlotting action that can cause an unwanted side effect called bleeding on the brain. Now, do we want to say—title a hearing, "Why Is the VA Giving a Bleeding on the Brain Inducing Drugs to Veterans?"

So you could go down almost every drug that has a side effect, and you can turn it into sensationalism and be inflammatory. I think that this Committee has a more important and responsible role here, and we should hear the testimony of our witnesses and their answers to our questions; and then, only after a careful inquiry, can we make informed judgments on what occurred and what corrective actions and followup, Mr. Chairman, may be called for.

Make no mistake, I concur with your issues on accountability and responsibility and the question of whether our veterans are being well served.

With that, I will yield back to the Chairman.

[The prepared statement of Congressman Buyer appears on p. 83.]

The CHAIRMAN. Thank you, Mr. Buyer.

I would just note that while most of us here do lack so-called expertise on the efficacy of drugs, we are experts in being parents, we are experts in being family members and we should be experts in being guardians of the veterans under our care. And there is no more important role than safeguarding those veterans.

And I will tell you, as a father, that if I read that Pfizer advisory and my child was on Chantix®, I would immediately tell them to stop taking the drug. I don't need any more expertise than that.

I want to, once more, thank *The Washington Times* for the articles and the continuing story. Many of our most important work on this Committee for the last year and a half has been sparked by the media doing its job; whether it was *The Washington Post* dealing with Walter Reed, whether it was *ABC News* dealing with traumatic brain injury, whether it was *CBS News* dealing with suicides, and all the other media out there that have looked at these issues and done the work that many of us see as our work for oversight on this Committee.

We thank *The Washington Times* in this case, but the media in general for watching out for our veterans.

Mr. STEARNS. Mr. Chairman, point of order, just a question, if I may.

Normally, in hearings of this magnitude, certainly all Members should generally have an opportunity for an opening statement. I was wondering, are we going to proceed in regular order in which each Member, both the Republicans and the Democrats, have an opportunity for a 3-minute, 2-minute opening statement? Is that possible? Many of us would like that opportunity.

The CHAIRMAN. We have four panels. But at your request, I will be happy to do that.

Mr. STEARNS. Sir, I'm not just asking for myself. I'm——

The CHAIRMAN. I'll ask everybody else.

Mr. STEARNS. Well, I think it is important.

The CHAIRMAN. Going down the rostrum—Mr. Mitchell, if there is any opening statement any of you would like to make. Mr. Mitchell?

Mr. MITCHELL. I'll submit mine.

[The prepared statement of Congressman Mitchell appears on p. 85.]

The CHAIRMAN. Mr. Hall.

OPENING STATEMENT OF HON. JOHN J. HALL

Mr. HALL. Thank you, Mr. Chairman. I'll just briefly say that the drug in question, I'm looking forward to hearing the testimony on.

I don't think, with all due respect to my friend, the Ranking Member, that aspirin, which is probably one of the most studied drugs in history, can be compared in terms of our knowledge and experience with it to this one.

But the underlying problem of undiagnosed and untreated PTSD is really the story here, in my opinion. And yet again yesterday *The New York Times* had a story about alcoholism and self-medication by veterans who sometimes had to go through fatal traffic accidents, bar fights, winding up in jail, domestic violence that they were arrested for, et cetera, et cetera, before they sought or were given treatment for PTSD, because they were taught to be tough

and to handle things and to deal with it as a man or as a woman. But it happens to be mostly men through the proportion in the armed services.

And we voted out of this Committee a bill, which would provide for—a presumed stressor for PTSD. It costs more not to treat it. In fact, the RAND study said that $6.2 billion in 2 years for undiagnosed is the cost to our society, to our country of undiagnosed and untreated PTSD—$6.2 billion in 2 years.

The Congressional Budget Office score for that section of the bill was $5 billion over 10 years. So it costs a fifth as much for us to treat it as it does not to treat it.

And I think that I will get back to the topic and allow the hearing to resume. But I hope that we'll all look at this in the big picture of medications that are being used to try to, in this case, stop smoking but are being used on people who—a large percentage of whom have undiagnosed and untreated PTSD. And that itself is a larger problem.

Thank you, Mr. Chairman.

The CHAIRMAN. Thank you, Mr. Hall. Thank you for your leadership on this.

Mr. Stearns.

OPENING STATEMENT OF HON. CLIFF STEARNS

Mr. STEARNS. Thank you, Mr. Chairman.

Mr. Hall, I have a list here from the *Physician's Desk Reference* which, as you know, is a physician's manual. There are over 200 drugs that are listed as suicide-related, and people who take these drugs will indeed have the feeling they should commit suicide.

So the Ranking Member, Mr. Buyer, mentioned aspirin. He could just as well have mentioned Albutirol, which people take for asthma. He could mention Paxil. I mean, they just go on and on and on. So Mr. Buyer is mentioning aspirin just to make a point, because I think his point is well taken. The title of this hearing is inflammatory, is not responsible; and here we are together as Republicans and Democrats and Independents looking to provide substantive credibility to this hearing. We don't want to start the hearing off with something that is so inflammatory it sounds like a campaign, a political campaign. This is not a political campaign. These are the lives of the men and women who are protecting us.

And to single out this drug is fine. I don't think there is anything wrong with having a hearing. But, Mr. Hall, if you want to read this list from the PDR, on almost every physician's table there are 200 at minimum that could cause suicidal thoughts, and they're listed right here. And I would venture to guess—and you and I are both adults—in our lives we've taken some of these drugs here and didn't even realize that they have a possibility of suicidal inclination.

The second point I would like to make is, the Department of Defense prescribes this same medicine to 67,000 military personnel. So this is not just something that the VA is doing. They are prescribing it to 32,000. So if we are really going to look at this, why don't we bring in some people from the Department of Defense and ask them, with 67,000 people, more than twice what the veterans

are using, why don't we look at this drug in terms of their history and how it has functioned?

Now, if you look worldwide, there are 1.3 billion people that smoke. Out of that, 7.5 million use this drug today worldwide. Now, the problem is we have about—just under 500,000 people that die from smoking every year in this country, and this is a leading cause of a preventable death. So anything we can do as Americans to get people to stop smoking, so that roughly 500,000 Americans will live is important.

So I think we have to put in perspective what we're trying to do here. Sure, we've got to ask the question, why would the VA prescribe a drug that could worsen or magnify the symptoms of depression and anxiety to patients suffering from post traumatic stress disorder? I think that is worthwhile. But let's put it in perspective—perspective in dealing with the Department of Defense, worldwide; and what we're trying to do in this country is get veterans off smoking because it is a preventable death.

Thank you, Mr. Chairman.

The CHAIRMAN. Mr. Hare.

OPENING STATEMENT OF HON. PHIL HARE

Mr. HARE. Thank you, Mr. Chairman. I'm going to be very brief.

You're right, I think we are all parents and want the very best not only for our children, but for our veterans. This Committee, as I understand, has oversight over the VA and I'm not as concerned about the title of the hearing as I am with what has happened here. I'm committed to working with my colleagues on this Committee to get to the bottom so we can ensure that our veterans are treated humanely.

As is mentioned, we have a report out that approximately 1,000 veterans per month are attempting suicide. Is this part of it? I don't know. I'm not a doctor; I don't claim to be. I just want to get to the bottom of what we're doing so we can try to put an end to this.

Every person on this Committee, Republican and Democrat, I think wants to see the very best care given to our veterans; and if there are things we need to look at, I think we need to do that.

But I especially hope to find out the policies and procedures regarding research in human subjects that we are following in designing this CSP No. 519 and what oversight, if any, was involved. I also want to know if patients were adequately informed of the hazards of Chantix®. Did the VA respond in a timely fashion to the early communication, the Public Health Advisory for Chantix®? And why was consent not revised after the FDA's early communication? Finally, given new evidence of the risk associated with this drug, should the drug continue to be used to treat veterans of post traumatic stress syndrome?

So the bottom line here for me today is to find out what happened and what can we do, Republicans and Democrat alike. And when the Ranking Member mentioned aspirin and my friend, Mr. Stearns, mentioned all these other 200 drugs that are available, they could all have side effects, some very, very, destructive side effects; the fact of the matter is, to what degree, and particularly dealing with veterans with post traumatic stress syndrome, does

this make this situation worse? That is what I really want to find out.

So what can we do to prevent the suicides that continue at record-breaking paces? My fear is, with more veterans coming back with post traumatic stress syndrome, this situation is going to get worse before it ever gets better.

Thank you, Mr. Chairman.

The CHAIRMAN. Mr. Boozman, any opening statement?

Ms. Berkley.

Ms. BERKLEY. Mr. Chairman, I'd like to associate myself with Mr. Hare's thoughtful remarks. I'm going to reserve my time for an opening statement and perhaps submit it in writing later, and I would like to get to the witnesses.

The CHAIRMAN. Thank you.

Mr. Lamborn. That's—okay, somebody next to you.

Mr. Rodriguez, I didn't see you. Mr. Salazar declined.

Mr. RODRIGUEZ. Just I'm ready to listen to testimony and look forward to it. My main concern would be to see how we can begin to hold the system accountable in terms of making things happen for our veterans and get to the witnesses.

The CHAIRMAN. Thank you.

Mr. Scalise.

OPENING STATEMENT OF HON. STEVE SCALISE

Mr. SCALISE. Thank you, Mr. Chairman. And the Ranking Member has a lot of concerns about the report. I definitely want to hear from the witnesses.

But I think our main concern should be about the process and if, in fact, accountability is going to show where the consent was requested because we have veterans that were being subjected to participation and testing, which is not something new. But it seems that there is a big gap in the consent process from all the reports that have come before us, a real concern about the process of making sure that the veterans knew what they were doing, those who chose to participate in the testing; and if, in fact, medical personnel let them know what the side effects were and if consent was garnered, because in a number of cases, they haven't been able to produce signed consent forms.

And the fact that veterans may have been participating in research studies without proper consent leads to a number of major concerns; and I hope that gets addressed in the testimony, and I definitely have some questions as we get into that section. So I look forward to hearing it.

[The prepared statement of Congressman Scalise appears on p. 85.]

The CHAIRMAN. Thank you, sir.

Mr. McNerney.

OPENING STATEMENT OF HON. JERRY MCNERNEY

Mr. MCNERNEY. Thank you, Mr. Chairman. This is an important hearing because it appears that established principles in patient treatment have been ignored or pushed aside. We want to know if this was done because these are veterans or not.

Any patient who is given a drug is entitled to know what the side effects are, especially if the side effects are life threatening and especially if the patients are particularly susceptible to those side effects.

Since these subjects are veterans and the drug was administered by the Department of Veterans Affairs, it is our responsibility to investigate if wrongdoing took place, either intentionally or unintentionally. It should be dealt with. And we need to make sure that procedures are in place to prevent unnecessary sufferings of our veterans.

Thank you.

The CHAIRMAN. Thank you.

Mr. Walz.

OPENING STATEMENT OF HON. TIMOTHY J. WALZ

Mr. WALZ. Thank you, Mr. Chairman, Mr. Ranking Member. Thank you to our witnesses.

Mr. Elliott, thank you for being here. That combat infantryman badge (CIB) gives you the right and the privilege to sit right where you are at and tell us this, because our responsibility is to make sure that what you did to earn that, make sure we are doing our responsibility on this end to care for you and your family once you return.

A special thank-you to the VA and to Secretary Peake for taking time to be here. No one is more committed to the care of our veterans than the Secretary, who is concerned when we have lapses in getting them fixed.

So I look forward to today's testimony because the VA, while it provides some of the best care in the world, also has a unique responsibility in providing research and especially in some of our most vulnerable populations of PTSD and so forth. So I'm very concerned on that.

Now, this incentive to do the research and to get it right, especially in preventive medicine, whether it be smoking or whether it be diabetes, the VA is a leader and has a real unique role in that.

So this issue of—if corners were cut or protocols were skipped, it is tragic in terms of what happens to our veterans in their care. But it is also tragic if a very valuable treatment is out there and it doesn't get a fair shake to be implemented.

So I do think—and I associate myself with some of the remarks that my colleague, Mr. Stearns, made—there is a responsibility for us not to hype this or engage in thinking that would be gratuitous in terms of what we're talking about on this drug.

But I also think it means we have a responsibility to ensure that the VA follows all of the accepted protocols and the ethical conduct of these for the very reason as I stated earlier, the care of the veterans, as well as protecting the research mission that the VA has.

So I'm very much looking forward to this, and I also thank you Mr. Elliott for showing the courage to be here today to try to help us understand this.

So I yield back.

The CHAIRMAN. Thank you.

Mr. Cazayoux.

Okay, our first panel has two witnesses, James Elliott and Lieutenant Colonel Roger Charles. Mr. Elliott is a veteran from the Iraq War, who was given Chantix® by the VA and suffered severe side effects while taking the drug. He is accompanied by a friend, Tammy Hilburn, who has helped him and done a lot of research on the issue.

Lieutenant Colonel Charles, is the Editor of *DefenseWatch*, and helped Mr. Elliott after his experience. So we look forward to your testimony.

I know again, Mr. Elliott, this is not easy. But I think you're taking a position that you want to help other veterans, and we appreciate your courage in doing that.

Mr. BUYER. Mr. Chairman, may the witnesses be sworn in today?

The CHAIRMAN. We haven't done that in the past, but I don't mind and I don't think the witnesses mind.

If you'll stand up, the two witnesses, and raise your right hand.

[Witnesses sworn.]

The CHAIRMAN. Thank you all.

Mr. Elliott, please.

STATEMENTS OF JAMES G. ELLIOTT, SILVER SPRING, MD (IRAQ WAR VETERAN); ACCOMPANIED BY TAMMY R. HILBURN, SILVER SPRING, MD; AND LIEUTENANT COLONEL ROGER G. CHARLES, USMC (RET.), VICE-CHAIRMAN, BOARD OF TRUSTEES, SOLDIERS FOR THE TRUTH FOUNDATION, AND EDITOR, *DEFENSEWATCH*, ON BEHALF OF EILHYS ENGLAND HACKWORTH, CHAIRPERSON, BOARD OF TRUSTEES, SOLDIERS FOR THE TRUTH FOUNDATION

STATEMENT OF JAMES G. ELLIOTT

Mr. ELLIOTT. Thank you, Mr. Chairman. I have submitted my executive summary, and the diagram clearly illustrates that there was a vicious web that I was caught up in. That diagram is not part of my official testimony, meaning that it is—I haven't been allowed to use it as a PowerPoint presentation. I know that some of the other witnesses will be having those type of presentations.

And that is really all I have to say. Thank you.

The CHAIRMAN. I'm sorry. You have no further testimony today?

[The prepared statement of Mr. Elliott appears on p. 86.]

The CHAIRMAN. Colonel Charles.

STATEMENT OF LIEUTENANT COLONEL ROGER G. CHARLES, USMC (RET.)

Colonel CHARLES. Chairman Filner, Honorable Members of the House Veterans' Affairs Committee, on behalf of Eilhys England Hackworth, the Chairperson of the Board of trustees of Soldiers for the Truth Foundation, I am humbled to appear before your Committee.

Recent events show that this oversight function of your Committee is critical to ensure that the well-being of our veterans is, in fact, the highest priority of the VA. These events demonstrate that without Congressional oversight, true concern for the well-being of our veterans can deteriorate into mere lip service of an indifferent and self-serving bureaucracy.

I note that you have scheduled a most impressive group of experts on various medical and ethical issues related to human subject experiments as conducted by the VA. I do not bring their expertise to this hearing. What I do bring is the experience of a career Marine Corps officer who believes our Nation has a sacred responsibility to care for those who have manned the ramparts of freedom on our behalf. I also bring the skepticism of a journalist who, for 18 years, has investigated misconduct by various Federal agencies in the areas of defense and national security.

Let me now turn to today's hearing. While studying the experience of Army combat veteran James Elliott, I was struck by three major questions. My first question relates to the Hippocratic Oath and a physician's first responsibility to do no harm. How then did the VA physicians involved in planning and conducting this drug study fulfill their duties under this pledge?

Here are some related follow-up questions to consider: Would these physicians have subjected their own sons or daughters to such a high-risk drug study? And would they have failed to have informed their own children of the substantial risks this study entailed?

My second question relates to the Nuremberg Code and the fact that informed consent of all human subjects in medical experiments is an absolute requirement under this code. As you may recall, it was the exposure of the most heinous and gruesome medical experts by Nazi doctors that led to enacting the Nuremberg Code.

Our country's own history has, unfortunately, too many examples of medical experiments on unwitting subjects. The infamous Tuskegee syphilis experiment is perhaps the best known of such shocking violations by physicians of their own Hippocratic Oath. I have attached to this statement a Knight Ridder press report, dated July 7th, regarding the Federal criminal prosecution of a former VA staff physician at the Stratton VA Medical Center in Albany, New York. The Federal prosecutor asked the court to sentence this former VA physician—and I quote—"to spend a year in prison for his role in a drug research scandal that killed at least one veteran and victimized dozens more," end quote. I have subsequently learned that this Committee had a major role in that investigation. If it pleases the Chairman, I respectfully request this article be included in the record.

The CHAIRMAN. So ordered.

Colonel CHARLES. My last question for your consideration involves the participants themselves, the veterans with PTSD who were recruited by VA staff to become the subjects of this drug study.

Why were members of a group who by the VA's own diagnosis were struggling to return to mental health normality selected for this study? The mental health of these veterans was known to have been what a layman would term "fragile." Special caution and prudence should have been invoked before exposing them to a drug study where, by definition, unknown factors risked further damage to their mental health. Instead, the very VA physicians trusted to help these vets regain a more normal mental condition enticed the vets to join a game of mental health roulette while withholding

critical information that would have permitted true informed consent to have been given.

Sir, this concludes my prepared statement. I stand ready to respond to any questions that the Committee Members may offer.

The CHAIRMAN. Thank you.

[The prepared statement of Lieutenant Colonel Roger G. Charles and the attached article, appears on p. 90.]

And if I may ask, Mr. Elliott, you have been diagnosed with PTSD?

Mr. ELLIOTT. Yes, Mr. Chairman.

The CHAIRMAN. And you're a heavy smoker?

Mr. ELLIOTT. Yes.

The CHAIRMAN. And how long were you taking Chantix®?

Mr. ELLIOTT. Less than 3 months.

The CHAIRMAN. And given the kind of advisories that have come out, that we have commented on, do you feel you were adequately informed of the side effects?

Mr. ELLIOTT. No, Mr. Chairman, not at all.

The CHAIRMAN. Would you mind describing the event that gave you so much publicity—probably unwanted—in terms of what happened to you?

Mr. ELLIOTT. The events of February 5th are very well documented, and that issue has been completely resolved in the courts.

The CHAIRMAN. In the what?

Mr. ELLIOTT. In the courts.

The CHAIRMAN. I mean, do you feel that the drug that you were taking helped provoke that or not?

Mr. ELLIOTT. I strongly feel that way.

The CHAIRMAN. And you believe that the drug led to this episode with the police?

Mr. ELLIOTT. That's correct, Mr. Chairman.

The CHAIRMAN. What would be your advice for other people taking the drug?

Mr. ELLIOTT. Anyone who is on an antidepressant should not take that drug. That would be my advice. Ask more direct questions to your doctor, demand direct answers, demand that this Committee help answer some of the questions that are going to arise.

The CHAIRMAN. Okay. Thank you so much.

Mr. Buyer.

Mr. BUYER. First by way of opening, let me thank both of you for your service.

Mr. Elliott, before starting Chantix®, had you tried any other smoking cessation aids or drugs?

Mr. ELLIOTT. Yes, Mr. Buyer, I did.

Mr. BUYER. Which ones?

Mr. ELLIOTT. Phase one of Smoking Cessation Program 519, it—the program that I signed up for, I began with the nicotine patch, 21 milligrams, and that did not work very well. It helped to a point, but it did not completely eliminate my smoking habit. And then from there, I went to nicotine gum and at one point, because my nicotine habit was extremely strong, I was given both in conjunction with one another.

Mr. BUYER. Can you define the word "strong?" How many cigarettes or packs a day did you smoke?

Mr. ELLIOTT. Two packs, pretty much two packs a day, 40 cigarettes.

Mr. BUYER. What type? What kind?

Mr. ELLIOTT. Marlboro Medium.

Mr. BUYER. Filtered or unfiltered?

Mr. ELLIOTT. Filtered.

Mr. BUYER. Are you still currently enrolled in a smoking cessation program?

Mr. ELLIOTT. Negative.

Mr. BUYER. Are you currently using any smoking cessation drug or aid at this time?

Mr. ELLIOTT. No.

Mr. BUYER. When you entered the study, do you remember signing an informed consent form?

Mr. ELLIOTT. I do remember that very well.

Mr. BUYER. At any time, did you sign an addendum to the informed consent form?

Mr. ELLIOTT. Absolutely not. That addendum was not sent until after this whole affair of February 5th. It was not actually sent until we had confronted them about the FDA warnings.

Mr. BUYER. Did your doctor at any time talk to you about the advisory that the VA had received from the FDA?

Mr. ELLIOTT. No, not one single time.

Mr. BUYER. Did your doctor at any time discuss with you a medical belief that your continuing use of cigarette nicotine—your continuing smoking would have an adverse impact upon their treatment for post traumatic stress syndrome?

Mr. ELLIOTT. No, they never said that by me stopping smoking it would help my PTSD diagnosis and symptoms.

Mr. BUYER. Let me ask, as a patient—you are in a program that will help you get better with your PTSD and cessation of smoking, and the purpose of the study is the medical belief that your smoking does not—that actually works against your PTSD treatment. Or didn't your doctor—so when you signed your original informed consent, wasn't that the purpose of your entering this program?

Mr. ELLIOTT. I entered the program, 100 percent, because I wanted to stop smoking. That was the one and only reason I entered that program.

Mr. BUYER. All right. But at this point, you don't recall conversations with your doctor with regard to how important it would be to do the cessation of smoking because they could better treat mental challenges?

You don't recall any of those discussions?

Mr. ELLIOTT. No. Those discussions never took place.

Mr. BUYER. Prior to the episode in which there was an arrest, did you have any success with Chantix®?

Mr. ELLIOTT. No, not at all. As a matter of fact, I had had a terrible reaction to it in the first week.

Well, Mr. Buyer, as far as stopping—you know, smoking cessation goes—yes, I had cut my habit in half overnight. It was miraculous, I will say this, Chantix® as far as more or less convincing

your brain that you do not want to smoke anymore, that you get no pleasure from it, it works well.

I—overnight my smoking habits were cut in half.

Mr. BUYER. Thank you, Mr. Chairman.

The CHAIRMAN. Thank you, Mr. Buyer. Just as a reminder, I'm going in the order of Members who were here when we started the hearing, in order of seniority, then those who appeared later.

Mr. HARE.

Mr. HARE. Thank you. How are you doing now, Mr. Elliott?

Mr. ELLIOTT. I have been better. I've been worse. Be more specific, please?

Mr. HARE. Pardon me?

Mr. ELLIOTT. Be more specific about how am I doing right now?

Mr. HARE. You're no longer taking the drug?

Mr. ELLIOTT. No, I have not taken Chantix® since February 5th.

Mr. HARE. So, since February 5th, how have you been doing?

Mr. ELLIOTT. Well, I now know that many of the side effects do not occur until after you stop smoking Chantix®. I believe they are known as "withdrawal symptoms." And I have vomited blood on occasion, had massive testicular swelling; I continue to have skin problems.

Mr. HARE. When you stopped taking Chantix®, I'm assuming you were still under a physician's care?

Mr. ELLIOTT. No, not really.

Mr. HARE. So you didn't go to a doctor and say, I now have all of these post——

Mr. ELLIOTT. I have, absolutely, yes. It should be—in my VA medical files.

Mr. HARE. What did the physicians say to you when you told them you were having all these problems after you stopped taking the drug? What was their response to you?

Did they give you——

Mr. ELLIOTT. "Thank you, have a great day," that was pretty much their response.

You know, in fact, their response was so—I feel it was so inadequate that, you know, I will be going for outside medical care.

Mr. HARE. You will or you have?

Mr. ELLIOTT. I will.

Mr. HARE. So, in your opinion, all these problems that you encountered after you stopped taking the drug, you relayed those to a physician, and they basically said, you're on your own, there is nothing we can do about this?

Or did they advise you to start taking the drug again? I am confused because the drug causes the problems, you have more problems after you stop taking the drug, you see a physician; if I'm correct, the physician basically tells you, go have a nice day?

Mr. ELLIOTT. As far as psychiatric help goes, no, my original prescribing doctor, who prescribed me the Chantix®, we have no relationship at all now.

The doctor who was assigned in her absence, he has never really given me any advice as far as any of this goes. Off the record, he has told me just to be strong, bear through it.

You know, we discussed the fact that, you know, my PTSD has actually gotten much worse—you know, a lot of the paranoia, the

things that the Chantix® increased, the PTSD symptoms that Chantix® increased, they have not, you know, decreased since I quit taking it, and in some cases, they may even be worse.

My primary care physician, him and I, we do not address psychological issues. That is not his place. But he has, you know—I have had good medical care at the VA since this happened, but none of it is related to psychiatric issues.

Mr. HARE. I don't want to get personal here, but you've been diagnosed with PTSD. Are you seeing a psychologist to help you with the PTSD? We spoke about the physical effects, but are you getting any help from the VA in terms of other treatments?

Mr. ELLIOTT. I have received no substantive PTSD treatment other than the fact that I was prescribed Citalopram years ago, and I continue to take Citalopram.

Mr. HARE. I know I'm out of time, but I hope you are given the opportunity to seek additional help, if need be. I appreciate and honor your service to this country; and I would hope that you would be able to find somebody that would be able to help you not only with the physical symptoms and the other things that you have, but also with your PTSD. Clearly that is something that you will be dealing with, I assume, for quite some time. I hope that you can find somebody that you have confidence in and that can help you as you move down the line.

Thank you, Mr. Chairman.

The CHAIRMAN. Thank you.

Mr. Scalise.

Mr. SCALISE. Thank you, Mr. Chairman.

Mr. Elliott, if you could describe the process that got you involved in the Chantix® study in the first place, the conversations with the VA, how did you come to participate in the study?

Mr. ELLIOTT. Well, it has been an ongoing study. I can't say how long it has been in place; but as far as I remember, while I have been at the Washington, DC, VA Medical Center, I have seen posters everywhere, you know, advertising this smoking cessation program in one form or another. There's different forms of this study going on. I was initially—well, let me step back a minute, sir.

The very first time that I met with a Veterans Affairs psychiatrist in Little Rock, Arkansas, his main issue of his and—his dialog and my dialog, what he was most concerned with was the fact that I smoked and I needed to stop smoking.

Mr. SCALISE. In relation to PTSD or just separately?

Mr. ELLIOTT. Just in relation to my life, my existence, I needed to stop smoking. That is all he wanted to talk about.

But as far as the DC-VA goes, like I said, I had seen the posters; I was well aware of this, but I really had no interest in it. At the time, though, my veteran counselor—he is not a doctor, he was just a counselor—he assured me that he himself was—had, is—was a long-time smoker and a lot of things they had to offer were truly beneficial to me and that maybe, just maybe, I should think about going into this program. We discussed those options for 6 months probably before I actually considered, you know, the reality of me entering into this program.

The only deal I was willing to make—you know, if that sounds appropriate, I was willing to make a deal. But I said, you know,

okay, I will go ahead, I will do this, you know, I trust you, but you and the hospital administrators that are in charge of this program, you have to guarantee me that you will be my assigned counselor rather than just they randomly assign me to someone, which is how it was described to me.

I wanted it—I wanted to hear it and see it in writing, if possible, that he would be my counselor.

Mr. SCALISE. Did you get that assurance?

Mr. ELLIOTT. That happened, and that's when I unofficially became part of the program.

Mr. SCALISE. To get to the—I guess the official part where you actually signed the consent form, you said you did sign a consent form. What were those conversations like in terms of side effects, in terms of how detailed did that conversation go before you signed the consent form to make you aware of what the potential side effects would be if you did start this process?

Mr. ELLIOTT. That consent form that I signed, it was strictly limited to nicotine patches and nicotine gum. That meeting lasted close to 3 hours, just as the consent form states.

It really did take 3 hours. They did most of the speaking until the very end. They took a lot of time explaining to me that this was a three-year program, they were more interested in long-term results rather than short-term results. They were well aware of the fact that most of the participants would take that $30 and immediately go out and buy cigarettes. They did not care about that whatsoever because they were interested in long-term results rather than short-term results and——

Mr. SCALISE. But did you sign a consent form for Chantix®?

Mr. ELLIOTT. No, never. Never. Never.

Mr. SCALISE. So when did you start taking Chantix®?

Mr. ELLIOTT. October 30, 2007, my prescribing psychiatrist, she, sort of on a spur of the moment, informed me that there was a new drug, and it was called Varenicline. I had never heard the word Chantix® until after February 25. She told me that Varenicline was a new drug; she didn't know very much about it, but it had some great results in getting people to stop smoking quickly and that it might possibly cause me stomach ailments and which, in fact, it did. It got me to puke blood.

Mr. SCALISE. But no talk about the other side effects?

Mr. ELLIOTT. There was no talk whatsoever, and I asked a lot of questions.

Mr. SCALISE. The final question would be regarding the FDA health advisories that came about periodically about the drug while you were taking it. Did you get any conversations, were there any conversations with your medical advisers at the VA about health advisories that came out from the FDA on Chantix?

Mr. ELLIOTT. No, but I did receive monthly appointment reminders to go in and fill out the questionnaire, of which I was given $30 for. I, a lot of times, didn't even cash those $30 vouchers.

Mr. SCALISE. Were there health advisories that came out during the time when you were taking the drug?

Mr. ELLIOTT. Say it again.

Mr. SCALISE. Were there health advisories that came out from the FDA during the time when you were taking the drug?

Mr. ELLIOTT. There were three, and I was not told about any of those until I requested that those FDA health advisories be sent to me.

Mr. SCALISE. After you stopped taking it.

Mr. ELLIOTT. After I stopped taking it.

Mr. SCALISE. But not during?

Mr. ELLIOTT. But not during.

Mr. SCALISE. That's all I have. Thank you.

The CHAIRMAN. Ms. Berkley.

Ms. BERKLEY. Thank you, Mr. Chairman.

Mr. Elliott, thank you very much for being here, and thank you for your service to our Nation.

You will forgive me, but I am having a hard time tracking this, so perhaps you will help me understand it.

You were being treated for PTSD by the VA?

Mr. ELLIOTT. Yes, ma'am.

Ms. BERKLEY. And how long had you been in the PTSD program?

Mr. ELLIOTT. Since spring, 2005.

Ms. BERKLEY. And you were a two-pack a day smoker and wanted to kick the habit, and in speaking with your psychiatrist, she suggested Varenicline? First you were on the patch, and then you were on the gum, and then the woman doctor suggested—and I am sorry, I didn't catch that, Varenicline?

Mr. ELLIOTT. Varenicline, Va-ren-i-cline.

Ms. BERKLEY. Okay, Varenicline, and you agreed to take the Varenicline?

Mr. ELLIOTT. Yes, ma'am.

Ms. BERKLEY. But they never gave you that; they gave you the Chantix® instead?

Mr. ELLIOTT. Chantix® and Varenicline are the same product. Varenicline tartrate is the active ingredient of what is commonly known as Chantix®.

Ms. BERKLEY. So the doctor said you didn't really know anything about it; you could suffer some stomach ailments; but that she had heard or read that this was a new drug that may very well help you kick the habit?

Mr. ELLIOTT. She did state to me that it was a new drug and—hold on. Yes, she stated that it was a new drug, and there were little—it was known to work very well, as far as smoking cessation goes.

Ms. BERKLEY. Okay, and then she prescribed it for you. You started taking it. Do you take it on a daily basis? A weekly basis? Several times a day? How does it work?

Mr. ELLIOTT. I received the medication, the Varenicline, in the mail approximately November 5th or 6th, 2007. And per the instructions, you know, I followed the instructions to a T. You know, I always do that. I am very interested in my own personal healthcare.

Ms. BERKLEY. Did you have periodic checkups with her, or did you go back with her and say—you know, did she say, how is this working? How are you doing? What's the effect of the medication on you? Did you have contact with this doctor again after she prescribed it?

Mr. ELLIOTT. I had a lot of contact with her, and the people in the actual clinic who I filled out the paperwork with.

To go back to your first question, I began taking Chantix®, very small doses, because it is a rather hard-core drug. I was told that much, that this is going to be a wallop to your neurological process, and I took half a pill for 3 days in the morning. I took half a pill for 3 days in the morning and the nighttime. And then I took one entire pill one time. And then the next day I took two entire—I took one full dose of the Varenicline.

The next morning, I, my whole body broke out in a rash, itching, scratching sensation.

Ms. BERKLEY. Did you report that?

Mr. ELLIOTT. Yes, I did. But, first, you know, I am not a doctor, but I knew that the only thing new that I had introduced into my system was the full dose of Chantix®, and it was such a miserable experience that I immediately said, you know, cease, cease fire. I stopped taking it.

And then, by chance, I had an appointment with my primary care physician three days later. He advised me—and I still remember his exact words to this day—he said, "well, Mr. Elliott, it looks like we finally found something you are allergic to. You should stop taking that."

Ms. BERKLEY. And you did.

Mr. ELLIOTT. And I stopped taking it for a month, until I saw my prescribing psychiatrist again. And she—you know, I almost told her verbatim the same exact story I just told you. She said, "well, that's not a long-term problem. If you were only—if you were not having any problems while you were taking half a dose, then go back to taking half a dose, because it——

Ms. BERKLEY. And that——

Mr. ELLIOTT. And that is rare, so just go back to taking half a dose and everything will be fine." And I did go back to taking that half dose for approximately two and a half months. And I suppose I am lucky that I wasn't taking a full dose; maybe, perhaps, I would be dead right now.

But in mid-January, I went in, I was having—I don't—it's hard to explain exactly what I was going through, but all my PTSD symptoms, you know, increased tenfold, and I tried to go in and make an emergency appointment with that doctor.

Her receptionist and I, you know, we knew each other on a name-by-name, face-to-face basis. And initially, she said, "all right, Mr. Elliott, I will let her know that you need to see her."

And so then I got a little bit more frantic, like, "man, you need to understand, this is a severe emergency. I need to see her or another doctor right now immediately."

At that point, she got out a pen and paper. She took notes and said, I will relay this immediately.

And, unfortunately, I never heard back from that psychiatric clinic at the VA hospital until February 5, after it was too late.

Ms. BERKLEY. All right.

Thank you very much.

The CHAIRMAN. Thank you, Ms. Berkley.

Mr. Stearns.

Mr. STEARNS. Thank you, Mr. Chairman.

Mr. Elliott, let me just thank you for your testimony.

We are all operating, as the gentlelady from Las Vegas has pointed out, she was trying to understand what drugs you were taking in addition to Chantix®. The Ranking Member, Mr. Buyer, had requested, under the Rules of the House and the constitutional oversight authority given to Congress, on behalf of both Democrats and Republicans, that staff be granted access to medical- and research-related records relating to Mr. James Elliott, and we were denied.

So that some of the questions the gentlelady from Las Vegas is asking and Mr. Scalise asked and I am going to ask are necessary because we have no medical record. We don't know about the interaction of other drugs, perhaps, at the time you were taking Chantix®.

But I do want to point out to my colleagues that Mr. Elliott is wearing a combat infantry badge. It's prominent on his lapel, so he is a war hero.

Mr. Elliott, can you just tell me where you served in Iraq and your rank, if you would, and then I have some questions. Just briefly tell that, because I do want to give you that opportunity. If you don't want to——

Mr. ELLIOTT. I was part of Task Force Bandit. I served mainly in central Iraq, and I was a specialist.

Mr. STEARNS. Okay. Some of the questions have been asked, and you seem to indicate that, while you were taking Chantix®, you perhaps had taken some other medication, and I think you mentioned something called Citalopram, is that right?

Mr. ELLIOTT. Citalopram.

Mr. STEARNS. Is that the generic name for C-e-l-e-x-a, Celexa?

Mr. ELLIOTT. Yes, that is true.

Mr. STEARNS. Did you know that that's part of the Prozac family, which is an antidepressant drug? Did you know that?

Mr. ELLIOTT. I knew that it was a serotonin reuptake inhibitor, yes.

Mr. STEARNS. So, at the same time you were taking Chantix®, you were also taking a drug, a Prozac family-related drug?

Mr. ELLIOTT. That's correct. And that was one of my primary questions to my attending physician was, how is this going to react with Citalopram and the other medications that I have been prescribed?

[The following was subsequently received from Mr. Elliott:]

Mr. Elliott has never taken Prozac. He is on Citalopram.

Mr. STEARNS. Mr. Elliott, I had an opening statement in which I mentioned the physicians' manual in which all the drugs that are listed can cause suicidal thoughts. And some of these, Prozac and Paxil and some of the drugs that you were taking are on this list that cause suicide.

I don't know if you knew that, the side effects, one of the side effects is suicide. Did the people who gave you this Prozac-related drug tell you that some of the side effects would be suicide—could be, could be, possibly?

Mr. ELLIOTT. The—the psychiatrist who prescribed me the Citalopram initially, in spring 2005, he was not concerned that I was a suicidal individual. We did speak about——

Mr. STEARNS. But you were taking that at the same time you were taking Chantix®?

Mr. ELLIOTT. That's correct.

Mr. STEARNS. Okay.

Also, I saw from the record that you started taking Chantix® in November of 2007, and it indicated you had some hives and some itching, and I think that was brought out earlier, that you did have some immediate side effects. Is that true?

Mr. ELLIOTT. That's true.

Mr. STEARNS. And did you tell the doctor about these side effects?

Mr. ELLIOTT. I did.

Mr. STEARNS. In February 2008, *The Washington Times* reported an incident. At that moment you were taking Chantix®, were you taking any other medication besides this Prozac-related drug? Were you, for example, drinking alcohol?

Mr. ELLIOTT. No.

Mr. STEARNS. Just yes or no.

Mr. ELLIOTT. Alcohol was not an issue.

Mr. STEARNS. No, it's not—the question isn't whether it's an issue. The question is, were you drinking alcohol at the time this incident was reported in *The Washington Times*. Just yes or no, and I remind you, you are under oath.

Mr. ELLIOTT. Yes.

Mr. STEARNS. You were drinking alcohol?

Mr. ELLIOTT. Yes.

Mr. STEARNS. Were you consuming a sufficient amount of alcohol that it might have, in your honest opinion, affected your judgment at all?

Mr. ELLIOTT. No.

Mr. STEARNS. Were you consuming alcohol that it would—well, maybe, let's just be frank. Had you had a lot to drink?

Mr. ELLIOTT. No. I had such a little amount to drink that the police—they didn't give me a breathalyzer. I was never charged with public drunkenness.

Mr. STEARNS. I understand, but the point is you were drinking alcohol at the time this incident was reported in the *The Washington Times*. You were taking Chantix®, and also you were taking a family-related drug, Prozac, at the same time, too. I mean, those are correct statements, aren't they?

Mr. ELLIOTT. They are.

Mr. STEARNS. Notwithstanding that fact, the Veterans Administration clearly had a responsibility to get your—a written approval, and I have here documents that you have signed showing that you have given extensive approval for the use of the patch. It's page after page where you have agreed to take these smoking-cessation drugs. If they had given you this form, would you have signed it? Because it seems like you signed all these other forms for the smoking-cessation drugs.

Mr. ELLIOTT. I did sign this form. I did agree to take the patch, and I don't believe the patch is considered——

Mr. STEARNS. No, but I am just saying that it appears that you were willing to sign forms because you wanted to stop smoking.

Mr. ELLIOTT. That's correct. I was willing to sign forms. Had they came with me with a part two form, which I—one can conjecture that that part two form would be the consent to take Chantix®.

Mr. STEARNS. Yes.

Mr. ELLIOTT. Maybe I would have. Maybe I wouldn't have. It would depend on how honest they were.

Mr. STEARNS. That's a very important point, that you were not given the opportunity to sign these forms; and, two, you weren't told sufficiently about the side effects. And I think that's the point.

I just want to conclude, Mr. Chairman, to ask Colonel Charles, are you aware that the study did not include Chantix® in the protocol until January of 2007? Yes or no?

Colonel CHARLES. No.

Mr. STEARNS. Thank you, Mr. Chairman.

The CHAIRMAN. Thank you, Mr. Stearns.

Ms. Brown.

Ms. BROWN OF FLORIDA. Thank you.

Mr. Elliott, first of all let me tell you that I want to thank you for your service to this country, and I want to thank you for coming today to share your story with us. And I hope you don't feel that you are in any way under the gun, because this—what you are doing will help us as we move forward with our responsibility as far as oversight is concerned.

I have one question I want to ask you, and then I want you to share something with us, but I want to know how you are doing. Someone else asked you this question, and what I mean by how you are doing, are you able to hold a job now? Are you—you know, how are you functioning?

Mr. ELLIOTT. I had to drop out of the university.

Ms. BROWN OF FLORIDA. Okay. So you were a student?

Mr. ELLIOTT. Yes, ma'am, I was a straight-A student.

Ms. BROWN OF FLORIDA. A straight-A student.

Right now, you are just in limbo?

Mr. ELLIOTT. That's one way to describe it.

Ms. BROWN OF FLORIDA. Yes, sir.

You mentioned that you were involved in a study, and it seems that it was a very controlled study. How long was this study going on? I mean, it was for years?

Mr. ELLIOTT. I don't exactly know, but I began going to the Washington, DC, VA Medical Center in February or March of 2006, and, you know, even from that time I remember seeing the posters all over the walls, but it was October 31 of 2006 that I became part of the program.

Ms. BROWN OF FLORIDA. Okay.

I have a real concern when you indicated that you contacted the office. You told them that you had an emergency situation, and it—there was no follow up, no contact, until you had a complete breakdown.

Can you explain why someone did not get back in touch with you right away? Did you go into the office?

Mr. ELLIOTT. Yes, ma'am. I physically went into the office.

Ms. BROWN OF FLORIDA. And no one followed up?

Mr. ELLIOTT. No.

Ms. BROWN OF FLORIDA. The Secretary is here. He is sitting behind you. What would you share with him as to how we could improve the system?

Mr. ELLIOTT. Well, it's a well known fact that the doctors are, you know, under a heavy burden. They have a large case load.

Ms. BROWN OF FLORIDA. You were in a controlled study. I mean, you know, you were limited. It wasn't a large case load. You were visiting with——

Mr. ELLIOTT. Good point.

Ms. BROWN OF FLORIDA. Yes, sir. You were visiting with the counselor. The list that my colleague gave of drugs that could cause certain problems, but that is, when you are just taking these drugs. But you were in a controlled state, you were seeing a counselor. This should not have happened to you.

Mr. ELLIOTT. I agree, ma'am.

I think that, you know, in the future, if a patient who is known to be 100 percent PTSD diagnosed, if he comes in in an extremely agitated state, he should be seen by someone, you know, on the spot.

Ms. BROWN OF FLORIDA. Absolutely.

Mr. ELLIOTT. Another comment I would like to make, ma'am, is that you cannot compare aspirin, the common drug aspirin, which is, I guess, it is part of the list of 200 drugs that can induce suicide. But aspirin is also 100 percent natural product. It comes from the bark of a tree. Whereas Varenicline tartrate is actually derived from one of the more venomous snakes on the Earth, and that is very well known throughout the research of alpha-bungaro toxins. Aspirin and Varenicline tartrate are not even in the same universe.

Ms. BROWN OF FLORIDA. I do understand that. But in addition to that, you were in a controlled study.

Mr. ELLIOTT. Yes, ma'am.

Ms. BROWN OF FLORIDA. In other words, you were constantly seeing doctors, and you were involved with the VA, as opposed to just taking a list of drugs and, you know, not knowing what reaction. Clearly, you were having reactions, and there should have been follow up.

Mr. ELLIOTT. That's 100 percent correct, ma'am. I was in a controlled study. They knew very well what risk I could be facing. They saw me quite often. We had contact both on the telephone, in the hallways, in official appointments, at all capacities. We were in pretty good contact with one another.

But when I reached out that one time, and that one time was the most important time, I was more—I had the door slammed in my face.

Ms. BROWN OF FLORIDA. And that is where the system broke down?

Mr. ELLIOTT. And that is where the system broke down.

Ms. BROWN OF FLORIDA. I apologize for that. We are going to talk with the Secretary about that.

Do you want to say anything to us about trying to imply that taking alcohol or having a drink or having a glass of wine could have contributed to this problem?

Mr. ELLIOTT. I believe that, you know, the two beers that I had earlier in that day, they may very well have saved my life. I was at such a point of confusion that, you know, due to lack of sleep, due to a chemical war going on inside of my head, that I just needed to relax so desperately badly that those two beers that I drank earlier in the day, you know, they did enable me to go to sleep, and they possibly defused the situation in a much needed way.

Ms. BROWN OF FLORIDA. Once again, thank you for your service.

Mr. Chairman, I yield back the balance of my time.

The CHAIRMAN. Thank you.

Mr. Boozman.

Mr. BOOZMAN. Thank you, Mr. Chairman.

Again, I want to tell you how much we appreciate your service to our country. My dad did 20 years in the Air Force. And I know the sacrifice on your part and your family's.

I think we have really got two things going on. We've got the study issue, whether this was appropriate and things. And then the other thing is it's one thing to initiate a study in good faith. It's another thing, perhaps, to have problems like you had as far as follow up. In other words, again, it doesn't matter what medicine you take or this or that. Sometimes there are problems with it. On the other hand, your other contention is that you didn't get good care once you started having reactions.

As far as the medication, this is an oversight Committee in the sense of looking into this. It's difficult in not knowing what medications you were taking. It appears that you were drinking some, taking the anti-anxiety medicine along with that.

We didn't get the opportunity to look at your medical records in that regard.

Did anyone else get to look at those? Did you share those with anybody else prior to the hearing?

Mr. ELLIOTT. No.

Mr. BOOZMAN. Okay. Very good.

Like I said, I appreciate your service, and, again, I think we really do have two things to look at the appropriateness of the study and then, again, whether or not you were adequately taken care of in the sense that, once you started having problems, were people there to follow up with?

Tell me about, very quickly, you being in and out of the VA system, how would you rate it? How would you, besides this instance, how would you rate the care that you have had through the years?

Mr. ELLIOTT. Excellent.

Mr. BOOZMAN. Very good.

Okay. I yield back—I yield to Mr. Stearns if he has got another question.

Thank you very much.

Mr. STEARNS. Thank you, Mr. Boozman.

I don't have another thing. I just have a question, if I could, for the Chairman and his staff. In light of Dr. Boozman's comment about the interaction of these drugs and that we really don't know anything and that, as Mr. Elliott has pointed out, he did not make his medical records public, the question is for the Chairman. Did you or your staff have any review, personally, on the records of Mr. Elliott?

Did you request them? Did you look at them to be sure that we had the full picture here, the interaction of all the drugs that he has admitted taking at the same time he took Chantix®?

The CHAIRMAN. No, I didn't. I did not think that I had access to those records or should have access to those records.

Mr. STEARNS. Well, as you know, as we pointed out in our letter to you, that you have the constitutional right to have access to them. And, in fact, the VA administration would have provided them to you, and you and your staff could have reviewed this so it wasn't necessary for us to be asking all these questions, which are very difficult for Mr. Elliott to be asked under oath. And I would just advise in the future that if we are going to have this type of hearing that the constitutional oversight responsibility is for you to review those records before we have the hearing.

The CHAIRMAN. Thank you, Mr. Stearns.

Mr. Rodriguez.

Mr. RODRIGUEZ. Thank you, Mr. Chairman.

And Mr. Elliott, let me thank you also for your service.

How long did you serve our country?

Mr. ELLIOTT. Three years and a few days, 3 years and 5 days. I didn't enlist, sir, until November 11, 2001.

Mr. RODRIGUEZ. Thank you for your service.

Let me ask you, Colonel, on, I guess, you know, as *DefenseWatch*, I guess you are an advocate, you know, on behalf of soldiers?

Colonel CHARLES. Yes, sir, that's one of our functions, yes, sir.

Mr. RODRIGUEZ. One of your functions. Let me ask you, in terms of this study, do you have any other information on the study in terms of any other problems that have come up with anyone else?

Colonel CHARLES. I have just seen in the general media reports of other incidents, episodes with that same drug. They have been covered in the general media, but I have not had any contact with other veterans that have expressed any concern.

Mr. RODRIGUEZ. Yes, apparently, this is something that has, you know, serious concerns, and I know that, in any system, you know, we have some difficulties that we have to—have you all come up with any recommendations as to what needs to occur, what needs to happen in terms of making it more transparent?

Colonel CHARLES. No, sir, I think the regulations are in place. My understanding, if they are appropriately implemented, there's usually not a problem. It's when people are not fully following their own protocols that we get these episodes, these events.

Mr. RODRIGUEZ. Let me just indicate that I think I have gone to a lot of hearings. This is one of the first hearings, and I think this is the second time that the Secretary has actually been here before they come up. So I do want to thank you for being here and listening to some of these comments, because the main thing we want to do is see how we improve on access to healthcare for our veterans and making sure we close some of those loopholes and some of the problems that might exist out there.

And we want to make sure, and we are fully aware of the fact that, as a Congress, that we have not in the past provided the appropriate resources that are needed in order to make that happen. We are hoping that we can close the gaps there and do the right things.

Do we have anything else on the study as to why it came about or, you know, on the actual study that has taken place and how long it's been in effect or anything?

Colonel CHARLES. Are you addressing that to me, sir?

Mr. RODRIGUEZ. Yes, sir.

Colonel CHARLES. I did not really follow this study in detail. I did the initial review of the material that Mr. Elliott and Ms. Hilburn provided, validated the authenticity, I thought, and then in passing the information to *The Washington Times* for further work.

Mr. RODRIGUEZ. Let me just ask you, I guess, one other question, as an advocate of our soldiers, what, if anything, you would have to recommend to us, things we can do to help improve healthcare to veterans?

Colonel CHARLES. Sir, I will just say that, from what I am hearing, that if we can get more people like Dr. Peake involved in taking these difficult jobs on at the highest level, I think veterans would be well served.

Mr. RODRIGUEZ. Thank you very much.

The CHAIRMAN. If you would yield for a second, and I think Secretary Peake will talk about this, there was an internal review provided, and I don't know exactly how many people there were, but of the people admitted to the VA, they found, who were taking Chantix®, 11 attempted suicides, 1 attempted homicide, 9 had suicidal thoughts, 6 suffered from hallucinations. But I think Secretary Peake will talk about that.

Mr. McNerney is next.

Mr. MCNERNEY. Thank you, Mr. Chairman.

I want to thank you, Mr. Elliott, for coming and testifying today. I can imagine how difficult this must be for you.

Did you start smoking while you were on active duty in the Armed Forces?

Mr. ELLIOTT. No, I smoked before that.

Mr. MCNERNEY. Do you remember the events of February 5th which led to your arrest?

Mr. ELLIOTT. Vaguely.

Mr. MCNERNEY. Vaguely.

Ms. Hilburn, were you with Mr. Elliott during the episode which led to his arrest?

Ms. HILBURN. Yes, sir, I was.

Mr. MCNERNEY. Did you feel when you were in that situation that your life was in danger or anyone else's life was in danger?

Ms. HILLBURN. I felt that James was so disoriented and so in instinctual combat mode, he had reverted almost to a mode in which he was in a combat scenario, that I felt that the car keys needed to be secured, and I asked him for the car keys. He was highly agitated, and I felt that, indeed, police assistance was necessary for his own safety and that of others.

Mr. MCNERNEY. Mr. Elliott, do you believe or have you been told that the memory or the lack of clear memory was due to the drug Chantix®?

Mr. ELLIOTT. No, I have never, no doctors or anyone have ever come forward and said that to me, but it's pretty well known that Chantix® can cause memory lapses, distorted time, the lack of memory, I guess, you can say.

Mr. MCNERNEY. Thank you.

The psychologist who prescribed the Chantix® to you was Dr. Hallie Lightdale. Is that correct?

Mr. ELLIOTT. Yes, sir, that's correct.

Mr. MCNERNEY. Was Dr. Lightdale a VA doctor or assigned in any way by the VA?

Mr. ELLIOTT. As far as I know, she was, you know, a VA employee. I mean, she was always presented to me that way. You know, but now that you mention it, you know, throughout my whole experience with this program, I met lots of people that I had never seen before; I had met them on a one-time-only basis. They were extremely interested in what was going on in my life on a day-to-day basis, my psychological state, et cetera. You know, this is especially in the end. This was a very degenerative type situation.

You know, there's a witness on this consent form that I signed who I never met. That person was not there, you know, which, you know, I didn't really become alarmed at that fact until afterwards, but, you know, who are some of these people that are in and out of my day-to-day medical care?

Mr. MCNERNEY. Good question.

Mr. ELLIOTT. Are they VA employees? Are they Pfizer employees? I have no idea. But to answer your question, I have always been under the impression that Dr. Lightdale was, indeed, a Veterans Affairs sanctioned doctor.

Mr. MCNERNEY. Did Dr. Lightdale ever recommend that you stop taking Chantix®?

Mr. ELLIOTT. No. She more or less seemed adamant to get it down my throat at any cost.

Mr. MCNERNEY. Since you have stopped taking that drug, have you noticed substantial change in your behavior?

Mr. ELLIOTT. Quite a bit, yes, yes, sir.

Mr. MCNERNEY. Well, one last question. Were the possible mental side effects explained to you before you started taking the drug Chantix®?

Mr. ELLIOTT. No, sir, not at all.

Mr. MCNERNEY. Thank you.

I yield back.

The CHAIRMAN. Thank you, Mr. McNerney.

Mr. Walz.

Mr. WALZ. Thank you, Mr. Chairman.

And thank you, again, Mr. Elliott.

I do think that it has been conveyed that some of the difficulties in these questions aren't about trying to sterily deconstruct your life, that concern for you as an individual is definitely amongst everyone in here, amongst those sitting behind you. And I applaud you for, again, as I said, the courage to come here. Because it's not just about you; it's about future veterans who may be put in the same position.

The goal of this Committee and those here is to try and provide that oversight to make sure it happens. When I hear you say you received excellent care, I am glad to hear that because I, too, believe that the VA provides excellent care. As I have told them

often, I am their biggest champion and harshest critic to make sure we get it right every single time.

In just a minute, you are going to have the Secretary of the VA who is going to come exactly where you are sitting, and he is going to raise his hand in exactly the same way, and he is going to talk about ways that we can improve this. And I think you heard Members talk about this. That's a very good thing. It's moving in the right direction.

So I don't want you to think this is about individual care and the deconstruction and the timeline of some of the things that we are asking. We are trying to gather the best information.

From my perspective, I think Mr. Boozman was summing this up right. I have grave concerns about the study itself, about some of the protocols that were in place, the common rule and some of those. Those will be dealt with, with the witnesses afterward.

The other thing that comes to my attention and one thing that I am equally or more concerned about is, what happened to your trust in the VA as it eroded and what led to a situation? And I can guarantee you, on the comments that you went there in what you considered to be an emergency situation, and not receiving immediate care; every time one of those situations is brought up, we will find every single minute of what transpired in that. You can be sure that we will go to that, and the VA will do that.

We had an episode in Minnesota that we were able to backtrack and put all the information together. Because there are two very important things that happen when something like that happens. If it turns out that the veteran is truly misserved like that, it's absolutely tragic. If something happens that the information that's conveyed to the public is not exactly the way it turned out, it ruins the trust in the VA system.

And I would tell you, I sit here as a 24-year veteran. I am a retired Command Sergeant Major in the Army. My concern for you and the troops is the paramount issue, and building trust is the single biggest factor in a successful unit, as you well know.

You trusted those people to watch your back as you were patrolling the streets and kicking doors and everything else that happened. We need to make sure that that same trust is felt for the VA.

So my concern—and what I would like to try to figure out here is—I am pleased that you entered the system. You went, and as you know, PTSD is the normal human reaction to an abnormal situation. So to be in that position is absolutely normal at what you went through.

How did you first go to the VA? I mean, why did you first enter the VA? You said you were there in the spring of 2005, and you were in Iraq in 2003 and 2004. Is that correct?

Mr. ELLIOTT. That's correct, sir.

Mr. WALZ. Okay, could you just explain to me how you got there and how that interaction went, with your first initial visits to the VA and how they started diagnosing PTSD and how they were treating that? Could you just briefly summarize, if that went the way you would like to think the system should work?

Mr. ELLIOTT. Well, my family immediately noted the changes in me from before I went into combat and the changes that were very

evident to them when I came back home to America, you know, after my Expiration of Time and Service (ETS) date. They strongly urged me to go and seek psychiatric help, and that is how I got into the system.

As I stated earlier on the record, my very, very first visit with a VA psychiatrist was unsatisfactory, to say the least. I mean, he wasn't concerned about my day-to-day life. He was only concerned with the fact—he wasn't concerned with my war-time experiences. He wasn't concerned about if I was going to make it home safely after the appointment.

His only concern was the fact that I had a very strong nicotine habit.

Mr. WALZ. The first consultation you had when you were going in and your family was concerned about PTSD——

Mr. ELLIOTT. Very, very, very first consultation.

Mr. WALZ. The conversation went right to smoking?

Mr. ELLIOTT. Yes, sir.

Mr. WALZ. Did it improve any after that? I mean, the subsequent consultations and things. Was there more of what you were hoping they would talk to you about, about the things you had seen or the ways you were feeling different or the reaction your family was having toward you? Did any of that start to come up then?

Mr. ELLIOTT. It didn't come up on that day, but I only saw that doctor one time. After that, I was—I spoke with the chief of psychiatry there at North Little Rock Veterans Hospital, and he immediately had me assigned to a new doctor, and everything went very well after that.

Mr. WALZ. Okay.

Well, again, I thank you for coming here. I appreciate your understanding of why these questions—they will benefit those that follow with the same situation that you are in, and that's what we are trying to get at.

So thank you.

And I yield back.

The CHAIRMAN. Thank you.

Mr. Mitchell.

Mr. MITCHELL. Thank you.

Mr. Elliott, it concerns me that the VA would participate in this kind of a study with participants who are suffering from PTSD and are on the narcotic morphine, both of which impair mental stability.

Do you now consider yourself to have been in the proper state of mind to participate in a medical study?

Mr. ELLIOTT. Say again, sir?

Mr. MITCHELL. Do you now consider yourself, after—do you now consider yourself to have been in the proper state of mind to participate in a medical study?

Mr. ELLIOTT. No, not at all.

Mr. MITCHELL. Again, I would like to, as everyone here has, thank you for your service and thank you for coming today.

I yield back.

The CHAIRMAN. Thank you, Mr. Mitchell.

Mr. Hall.

Mr. HALL. Thank you, Mr. Chairman.

I, too, would like to thank you, Mr. Elliott, for your service to our country and offering you my best wishes and blessings as you go forward, and hopefully things will get better from here, and thanks for sharing your experience with us.

I actually wanted to ask Colonel Charles just one question. Should, in your opinion, the VA be putting soldiers or veterans who have been diagnosed with PTSD into test studies of new drugs of which one of the side effects is predicted to be possible suicidal tendencies?

Colonel CHARLES. Congressman, that's a very difficult question to make just a broad general answer to. I think you have to look at the specifics of each individual, but I will say that it raises the bar, in my mind, to a very high level before you can justify putting someone, who is already struggling for mental normality, into a drug study where one of the known side effects is a threat, a risk to that very mental normality.

So I wouldn't make a blanket statement, because there are many pressing medical needs out there and so on, but I would say the burden is on somebody to show why the risk is justified in this case.

Mr. HALL. All right, and I would acknowledge the validity of my colleague, Mr. Stearns, and Mr. Boozman's point about the different drugs that we take for different things, and sometimes it's a risk-benefit analysis. There may be another condition, physical or mental or psychological, that's being dealt with, and the doctor or psychiatrist needs to make these judgments.

But since one of the symptoms of PTSD is an increased likelihood of suicide attempts, it seems that that bar, as you say, should be raised for a drug study where the side effect of that drug may include the same thing. It could be a multiplier.

Thank you very much.

Mr. ELLIOTT. Yes, sir.

Mr. BUYER. Will the gentleman yield?

Mr. HALL. Yes, I would.

Mr. BUYER. You kept referring to this as a drug study. This was not a drug study.

I yield back to the gentleman.

It's a smoking cessation study. It's not a FDA drug study.

The CHAIRMAN. But the VA was trying to decide which patient was the best for the drugs.

Mr. HALL. Reclaiming my time, I would just say that I accept the point but would just say that a smoking cessation study, which is employing certain drugs——

Mr. BUYER. That's correct.

Mr. HALL. Nonetheless gives the medical people, the VA, the option to determine which drugs to use, but, more importantly, which veterans to put in the study, and I think that's my point.

Mr. HARE. Would the gentleman yield?

Mr. HALL. I would yield whatever time is left.

Mr. HARE. Thank you. I am confused here.

Mr. Elliott, if I understand you correctly, you went to the VA initially for PTSD.

Mr. ELLIOTT. Yes, sir.

Mr. HARE. And, the answer to PTSD was smoking cessation?

Mr. ELLIOTT. From the very first day it seems apparent to me that they were very interested in my smoking habits.

Mr. HARE. So you go to the VA, and you say, I think I have this problem; I need to see somebody. You are diagnosed with PTSD, and you're prescribed smoking cessation. But instead of beginning something that would treat the PTSD, they want to stop your smoking; is that what you are saying?

Mr. ELLIOTT. That's what I was saying.

Mr. HARE. I find that very confusing.

Mr. ELLIOTT. It's confusing. It's incredible. It's scary. It's sad.

Mr. HARE. Thank you, Mr. Chairman.

Mr. HALL. If I could, in just the couple of seconds that remain of my time, reclaim it and say that this was officially, PTSD and Smoking Cessation Study Number 519, just for the record.

I yield back.

The CHAIRMAN. Thank you, Mr. Hall.

Mr. Snyder.

Mr. SNYDER. I just want to thank you all for testifying today.

I don't have any questions, Mr. Chairman.

The CHAIRMAN. Thank you.

Mr. Elliott, you have heard all of our questions. Is there any last statement you would like to make, any observations, or any advice for us as we proceed to hearing from the VA and other witnesses?

Mr. ELLIOTT. Well, I agree with Lieutenant Colonel Charles that human testing at the VA hospital should be eliminated. And I would like to point out that the graph that is part of my executive summary, you know, it clearly shows a criminal network and motive, and, you know, that motive is money. And that's all I would say.

Thank you, Mr. Chairman.

The CHAIRMAN. Thank you, Mr. Elliott.

Mr. Charles, any last statement?

Colonel CHARLES. Mr. Chairman, I would just like to thank the Committee for their attention, and I hope, on a bipartisan basis, working with General Peake, you all will be able to solve what seems to have been a serious problem, and we hope it's not a big problem.

The CHAIRMAN. Thank you.

We thank you for your help in leading Mr. Elliott to ask the right questions.

And as everybody has said, we thank you, Mr. Elliott. We know it took a lot of courage, and it's not the easiest thing to share your personal story. We appreciate it very much.

We will adjourn this panel and move on to panel two.

Mr. ELLIOTT. Thank you.

The CHAIRMAN. Secretary Peake, thank you.

To be consistent with Mr. Buyer's request, if all the witnesses will please stand and raise your right hand.

[Witnesses sworn.]

STATEMENTS OF HON. JAMES B. PEAKE, M.D., SECRETARY, U.S. DEPARTMENT OF VETERANS AFFAIRS; ACCOMPANIED BY JOEL KUPERSMITH, M.D., CHIEF RESEARCH AND DEVELOPMENT OFFICER, VETERANS HEALTH ADMINISTRATION; J. THOMAS PUGLISI, PH.D., CIP, CHIEF OFFICER, OFFICE OF RESEARCH OVERSIGHT, VETERANS HEALTH ADMINISTRATION; MILES MCFALL, PH.D., DIRECTOR, POST-TRAUMATIC STRESS DISORDER TREATMENT PROGRAMS, VETERANS AFFAIRS PUGET SOUND HEALTH CARE SYSTEM, VETERANS HEALTH ADMINISTRATION, U.S. DEPARTMENT OF VETERANS AFFAIRS; AND PAUL SELIGMAN, M.D., M.P.H, ASSOCIATE DIRECTOR OF SAFETY POLICY AND COMMUNICATION, CENTER FOR DRUG EVALUATION AND RESEARCH, FOOD AND DRUG ADMINISTRATION, U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES; ACCOMPANIED BY ROBERT TEMPLE, M.D., DIRECTOR, OFFICE OF MEDICAL POLICY, CENTER FOR DRUG EVALUATION AND RESEARCH, FOOD AND DRUG ADMINISTRATION, U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES

The CHAIRMAN. Secretary Peake, we thank you, and appreciate knowing that you were paying very close attention to the testimony.

Joining you today is Dr. Joel Kupersmith, the Chief of Research and Development; Dr. Thomas Puglisi, the Chief Officer of Oversight Research; Dr. Miles McFall, the Director of the PTSD Patient Care Line at VA Puget Sound Health Care System. Also joining you is Dr. Seligman who is the Associate Director of Safety Policy and Communication, Center for Drug Evaluation and Research for the Food and Drug Administration.

I am sorry—that was Dr. Seligman, and he is accompanied by the Director of the Office of Medical Policy, Dr. Robert Temple.

We thank each of you for being here. It's a very important issue, and we thank you for your testimony.

Secretary Peake, you are recognized.

STATEMENT OF HON. JAMES B. PEAKE, M.D.

Secretary PEAKE. Mr. Chairman, I have a statement to submit for the record with your approval.

The CHAIRMAN. So ordered.

Secretary PEAKE. Mr. Chairman, Congressman Buyer, Members of the Committee, thank you for holding this hearing and for the opportunity to discuss the important issues on our use of FDA-approved medicine, of our Cooperative Study Research Protocol No. 519 and of the integrity of our research programs.

The issues raised are integral to the care of our veterans today, to their best care in the future, and to our absolute obligation to them for the quality of that care and maintaining a research system that keeps their well-being and safety as an unequivocal priority.

That makes it particularly painful to hear Mr. Elliott's experience with PTSD and some of his perceptions about VA care.

I was appreciative to read in the paper 2 weeks ago the accolades he gave for those who provided care at the VA and to hear him today, again, talk about, today, the excellent care.

While I was appalled to hear about his experience in seeking emergency care—and I can guarantee you, I am going to look into that—regarding the medication Varenicline and its use in helping veterans stop the dangerous and addictive behavior of smoking.

First, Varenicline, also known under the brand name of Chantix®, the same thing, has been FDA-approved since May of 2006. It has been widely prescribed in the United States and overseas since that time.

The VA, after usual consideration, which is significant, and review, 8 months later placed it on the national formulary, January 2007. This is a prescribed medicine, which means that the decision for its use is an individual decision between the patient and his or her healthcare provider.

Just as with any prescribed medicine, the provider, with the patient, weighs the potential benefits of a medicine against any potential side effects.

In the case of Varenicline, it has been considered a medicine primarily, as you heard, for those who have failed other forms of smoking addiction assistance. Tobacco use remains the single most preventable cause of morbidity and mortality in the United States. Stopping smoking before the age of 50 reduces the risk of death by 50 percent over the next 15 years.

The CHAIRMAN. Secretary Peake, I shouldn't interrupt you, but you had the benefit of listening to the earlier testimony.

Secretary PEAKE. Yes.

The CHAIRMAN. When something is directly dealing with something that you are saying, I would ask you to address it, because you said that there has to be close consultation with a doctor and a patient about the side effects. The testimony was that there was no such thing.

I think you need to address those issues as you bring them up and not just wait for us to say——

Secretary PEAKE. I can address that now, or I can complete my statement.

In fact, I did listen to, very carefully, Mr. Elliott, who talked about being, in consultation, in November, with his physician, told about the side effects of nausea, stomach upset——

The CHAIRMAN. He testified he was not told of the side effects of Chantix®——

Mr. BUYER. I would ask for regular order——

The CHAIRMAN [continuing]. And he was given no consent form to sign.

Mr. BUYER. I ask for regular order and permit the Secretary to testify, Mr. Chairman.

The CHAIRMAN. I am the Chairman, and I am following the regular order.

The testimony was that there was——

Mr. BUYER. The rules decide the regular order of the Committee, Mr. Chairman.

Allow the Secretary to testify.

The CHAIRMAN. The rules do not allow you to interrupt.

Mr. BUYER. Allow the Secretary to testify, I think is what the Committee would like.

The CHAIRMAN. Secretary Peake, the testimony stated that there was no such explanation of the side effects, and there was no consent form. You stated that the process is that there should be such consultation. So, please address that, sir.

Secretary PEAKE. Sir, this was, as the Ranking Member pointed out before, not a drug study. There is, there was not a separate consent form for Chantix®, which was an FDA-approved drug that 32,000 people—70,000 people, actually, across the VA, 32,000 currently, are getting in consultation with their individual physicians.

The CHAIRMAN. How many of those have PTSD?

Secretary PEAKE. About 6,000, sir.

And what I would—as I listened to the testimony, the side effects that were described, when Mr. Elliott started, was started on Chantix®, were the side effects that were known at the time, and that was specifically as he talked about, nausea and so forth. I mean, that's——

The CHAIRMAN. Yes, but other side effects became known later, and he said he wasn't informed about them. So address the issues here, not just what was——

Mr. BUYER. Regular order, please.

The CHAIRMAN. Stop interrupting me, Mr. Buyer.

Mr. BUYER. Regular order. I ask for regular order.

The CHAIRMAN. Secretary Peake, you said he——

Mr. BUYER. I ask for regular order for Mr. Secretary to testify.

The CHAIRMAN. I heard you, Mr. Buyer.

He is at the Committee. I am asking a question about his testimony.

Mr. BUYER. I asked the Secretary to testify. Please do not be rude. There are three equal branches of government. This is a Secretary of a department of the government.

Please do not be rude to the Secretary.

The CHAIRMAN. I am not being rude to the Secretary. I am asking him to explain why he keeps saying that there was this process. We heard testimony that the process was not followed. Please address that point, sir.

Secretary PEAKE. Sir, if I could explain the nature of this study, it might be helpful.

The nature of the study was, had nothing to do with the drug. It could take any medicine that the doctor, that his doctor would prescribe to help him to stop smoking. I believe Mr. Elliott explained that.

The issue of the study was solely about whether you received that smoking cessation medicine or counseling or therapy from your PTSD provider or in a venue other than your PTSD provider.

The medicine, sir, was prescribed based on what you and your doctor decided was best.

The CHAIRMAN. But new warnings had come up?

Secretary PEAKE. Sir, I can address—I would like to talk about the sequence of the warnings, if you would like.

The CHAIRMAN. Okay.

Secretary PEAKE. And on 19—but I should tell you that on 19 November, the Medical Letter on Drugs and Therapeutics, one of the most widely read and authoritative sources used by clinicians for current information on medications, updated their previous

comments on smoking cessation, stating: More recent publications and the clinical experience of the Medical Letter consultants now suggests that Varenicline is the most effective drug available for this indication, more effective than nicotine replacement therapy or Bupropion, which is Zyban.

In that same report, the Medical Letter did add, and I quote, "a word of caution: Exacerbations of psychiatric illness have been reported in patients who took higher than recommended starting doses of Varenicline."

Related to this word of caution, they refer to two case reports, one of an exacerbation of schizophrenia and another of a manic episode in a patient with bipolar disorder.

There's no recommendation to not use the medicine. On 21 November, 1 day later, the FDA did issue an early communication on Varenicline.

This is a source of information to clinicians to help inform their individual prescribing practices. Unlike a provider in private practice, who must keep up with this kind of information on their own, the VA provides this kind of information retransmitted through our pharmacy program, just as they did in this case, one day later on the 21st of November. This early communication is not a drug alert, not a warning.

It suggested that healthcare professionals monitor patients for behavior and mood changes; that patients contact their doctors if they experience behavior or mood changes; and that patients use caution when driving or operating machinery.

On 18 January of 2008, further information was similarly distributed to VA healthcare providers reporting on Pfizer's labeling changes and the European Medicine Agency's preliminary warning noting that Varenicline should be reserved for—as we told them—for veterans who have not been successful with or for whom nicotine replacement therapy are contraindicated; also that the healthcare provider should educate veterans about the changes in behavior or mood and instruct them to report such changes to the provider.

Again, this information was provided to our clinicians to have them better informed so that they, in conjunction with their patient, can make the best clinical decision.

On 1 February, the FDA issued a public health advisory for healthcare professionals to highlight revisions to the warnings and precautions section of the full prescribing information for Chantix® regarding serious neuropsychiatric symptoms. These symptoms included changes in behavior, agitation, depression, mood, suicidal ideation, and attempted and completed suicides.

Specifically noted on the Web site was that the FDA is not advising practitioners to discontinue prescribing the product.

There was not then, nor is there now, a black box warning or a product recall on Chantix®.

On 5 February, based on this updated information, the VA's pharmacy benefit management—that's 4 days later—our Benefits Management Service issued an alert through the pharmacy channels to all of our clinicians so that all who might be prescribing Varenicline were aware of the updated information and specifically the recommendations that patients tell their doctor about any his-

tory of psychiatric illnesses prior to using Varenicline, that healthcare professionals, patients, patients' families, caregivers be alert to and monitor changes in mood and behavior in Varenicline and that Varenicline patients immediately report changes in mood and behavior to the doctor. This information went to clinical staff, VA smoking cessation lead clinicians, Smoking and Tobacco Use Cessation Technical Advisory Group, the Medical Advisory Panel, pharmacy chiefs, chief medical officers and clinical pharmacists. You know, this drug was officially added to the VA national formulary, as I said, in January of 2007. Concurrently, VA reviews of Varenicline were begun in the VA focusing on dehydration and a Atrial fibrillation that were the things that we knew at that time were associated with Varenicline.

In October of 2007, we were seeing some reports of psychiatric issues in patients on Chantix®. Data at that time suggested just under one-half of 1 percent had such symptoms reported. These are through the adverse drug event reporting system that we had. In December of 2007, our VA Med Safe Group instituted a rapid cycle analysis as we watch lots of different medications to look at adverse events, laboratory findings, International Classification of Diseases (ICD)–9 codes, Current Procedural Terminology (CPT) codes, mortality data from administrative databases. From December of 2007 through March, that data was analyzed. From March to May, VA developed and vetted and published Varenicline formulary prescribing and guidance. In the meantime, the medication label, which goes on each container, was updated in December of 2007 and again following—and I think we have a copy of that there up on the screen—was updated again in February. So that every bottle that came had that warning appropriately on it.

The point, Mr. Chairman, is that there has been a lot of due diligence about this medication. Medical professionals engaged in each step along the way to assist providers to appropriately use this medicine for their patient, making that individual decision with the best information available. And again, it is for not just those in the study, but for the 32,000 folks, 6,000 of which have PTSD that are out there trying to stop smoking.

This is very important as I turn now to the issue of the cooperative studies program, Protocol No. 519. It is a study designed to find the best venue to provide smoking cessation assistance in patients with stable PTSD. Can I have that next slide? This is not a study of this drug or any other drug. It can be just counseling for that matter if that is what your doctor thinks you need. All therapy is between the healthcare provider and the patient using only FDA approved medicines in association with counseling. There was no investigational drug involved. The smoking cessation complement can be provided either in the PTSD treatment venue or in another smoking cessation venue.

At the beginning of this study, Chantix® was not even on the market and that was back in 2004. When it became FDA approved and available as part of the armamentarium for providers in general to use in smoking cessation, it became one more tool for the individual provider and the patient to use to help stop smoking. All of the information on this medicine and the updates, so that information from the post marketing experience was available to the cli-

nicians caring for our veterans in this study. In addition, because of this study, additional consideration—really because of the study—I want to emphasize that—additional consideration was given to first the early communication with discussions by medical professionals, seriously considering this issue, aware and experienced with dealing with veterans in this study and patients with PTSD in general.

On 26 November, again on 4 December, they had conference calls of the Cooperative Study Group. And it was their considered opinion that there should be no recommendation to alter the study at that time. Following the February alert, the Cooperative Studies Group in addition to immediately forwarding the alert through research channels again had discussions to further consider this new information consistent with the promise to update veterans in the study on new information on smoking cessation, an addendum to the consent form was produced and a draft letter, the wording of which was carefully considered, encouraging patients to follow up at the next study visit to discuss and to report immediately any changes in mood or behavior or a desire to discontinue Chantix®.

This letter itself did not contain the word "suicide." I acknowledge that. However, the addendum to be attached did have the full description of the alert to include the word "suicide."

Each study location has an institutional review board (IRB) responsible for ensuring that the research done at that institution is ethical and meets the scientific standards required. The IRB has the final say in the conduct of such research to include materials sent to patients, the content of the consent and other informational materials, and consider the guidance that comes from the Cooperative Study Group in such a multi-institutional research study as this.

Ultimately, each IRB, as was done at the Washington VA, approved the letter and addendum with the appropriate local information added and points of contact to be sent to the patients in the study.

Turning back to the title of this hearing. As we have reviewed this study, including those study subjects who had obtained Chantix® from any VA source, we found 241 who had been on Chantix® at some time during this study. The only two deaths in this group was one from liver cancer and one from coronary artery disease, neither in any way potentially related to Chantix®. There were no deaths from suicide in this group. Of the 241, there were 19 veterans who had sometime during the study, reported one or more psychological adverse events, to include 11 who reported some level of suicide ideation. I would point out that in any study reporting of adverse events includes any event that happens to the person in the study and is not necessarily causally related to the study at all or to any particular medicine in the study.

And if I can have the next slide. We watched these serious adverse events from the very beginning of the study out to May. You can see that it is relatively constant and you can see when Chantix® was started and you can see there wasn't any big—or statistical bump to make us think that there were some real worrisome thing. The next piece is—you know, the ordinate is—the Y axis there is important. This is .01 percent, is that first grid line,

and this is the psychological issues that were reported in terms of serious adverse events (SAEs) in this study. You see a little bump there at the right-hand side of the graph? It is right after the FDA warning came out. I think people are more alert to those kinds of things. But, again, that is at the .01 percent level. Next line. Currently there are only 40 who are prescribed Chantix® that are under the care of a provider in this study. Over the same period of the study in this population of patients with PTSD, of the 704 veterans not on Chantix®, 28 experienced psychological adverse events, one completed suicide and one died of an intentional overdose yet to be characterized as a suicide. And that was among over the course of the study 25 total deaths.

All of this information has been reviewed by the Data Monitoring Committee who fully aware of the concerns, concluded that the actions that we have taken and that have been taken have been the right ones.

I have spent a fair amount of time to lay out the particulars in this case, sir, and I appreciate your indulgence. I do fully appreciate the unique population that we serve and the importance of the research to ensure that their unique needs are appropriately studied and that we apply the best evidence-based medicine on their behalf. Far from considering our veterans as Guinea pigs or disposable heroes, as has been suggested in some of the headlines, they are a precious national resource and they deserve the best of science and medicine by people who care about them and people who understand their sometimes unique characteristics and needs.

I know you share this concern and our Ranking Member particularly pushed to reform our research institutions establishing Dr. Puglisi's organization, the Office of Research and Oversight (ORO). Over time, we have put in place a structure with this ORO oversight and the Office of Research Development, institution review boards and cooperative studies human rights Committees that absolutely can support the finest scientific inquiry and the proper considerations and safeguard of our veterans while meeting their needs.

However, I will tell you, excellent structure must be matched with excellent execution. And while I believe the appropriate decisions and considerations were ultimately made in the course of this study, I have directed a detailed review, not only of this study, but of all ongoing studies involving our veterans with PTSD.

Our Office of the Inspector General has reviewed the execution at the Washington VA around this study, specific concerns have been raised about the thoroughness of the patient contact, ready availability of information on and about study subjects and of the quality of the study audits. In one instance, a research misconduct inquiry has already been directed to investigate an allegation of improper data collection. Each of the OIG findings and each of their recommendations will be examined and acted upon. Their work will inform the ongoing review that I have already directed and their additional investigation will be complementary and a complete review for me to understand what additional safeguards in our research programs should be implemented.

Further, where we find inadequacies, I will demand institutional and personal accountability. That is what we owe to our veterans and that is what we owe to the American people.

I listened carefully to Mr. Elliott. It hurts me when any of our veterans suffer like that. And while I do not agree at all with his feeling that the VA should not be engaged in research, I do believe that in the research we do have a special responsibility and we must go that extra mile.

Mr. Chairman, I thank you and I look forward to your questions.

[The prepared statement of Secretary Peake and slides appear on p. 92.]

The CHAIRMAN. Thank you. Dr. Seligman?

STATEMENT OF PAUL SELIGMAN, M.D., M.P.H.

Dr. SELIGMAN. Mr. Chairman, I do have a very brief statement to make. As you know, I am here today on behalf of the Food and Drug Administration Center for Drug Evaluation and Research, and I am joined by Dr. Robert Temple, who is the Director of Medical Policy.

As you know, FDA is responsible for the regulation of prescription and over-the-counter drugs that play an increasingly important role in improving and maintaining our health. FDA's oversight responsibilities for drugs include pre-market testing, evaluation of drug applications and, where appropriate, approval of drugs for marketing. It also includes post-marketing monitoring of drug safety and communicating information to healthcare professionals and patients to help guide their decisions in the safe and appropriate use of drugs.

FDA's drug review process is considered and recognized to be the worldwide gold standard. We incorporate the latest advances in medical science in our reviews, which include a complete assessment of the drug's metabolism, its interactions with other drugs, and potential differences and effectiveness and safety in people of different genders, ages and races.

All drugs, as you know, carry risks and can cause side effects. A critical aspect of evaluating the safety of drugs and assuring their most appropriate use is the effort to assess drugs after they are approved. No amount of pre-market study can discover all we need to know about a drug's effectiveness or its risks. New safety problems are regularly identified when a new drug is used by the general population in larger numbers than studied in pre-market.

FDA's post-marketing monitoring program plays an essential role by collecting and assessing information about adverse events and medication errors identified after approval. We learn about these effects in various ways, but mostly from reports from physicians, nurses, pharmacists, healthcare institutions and other providers sent directly to the FDA or via the drug company. We now receive almost a half a million reports a year for all drugs nationwide. We evaluate these reports together with information from other sources as available, as part of our continuous assessment and reassessment of the balance between the benefits and risks of the product. Our response to information from this ongoing surveillance depends on our evaluation of the aggregate public health benefits of the product compared to its evolving risk profile.

FDA also uses a broad range of methods to communicate drug safety information to the public. Certain forms of communication are targeted to specific audiences such as physicians or patients. Others are directed to more than one group to ensure their widespread dissemination.

The FDA approved drug product label is the primary source of information about a drug's safety and effectiveness. It summarizes the essential scientific information needed for the safe and effective prescribing and use of the drug. Labeling for prescription drug products is directed primarily to the healthcare professional but often includes patient counseling information as well. As we learn new information about the safety of the drug, we update the section of the label that lists the adverse events and that describes the warnings and precautions for its use.

More information going directly to the patient is considered important. It can be provided in the form of a medication guide or a patient package insert that accompanies the dispensed drug. In addition to the professional label, FDA uses a variety of means to communicate important often emerging safety information.

As Mr. Secretary pointed out, we use public health advisories, which are directed to help patients and healthcare professionals and the general public and are used to highlight important safety information. We also use healthcare professional information sheets again to communicate important information and to provide recommendations to mitigate potential risks.

Since August of 2007, FDA has issued early communications about ongoing safety reviews to keep healthcare professionals and the general public informed of post-market safety issues that are currently being evaluated by the FDA. Early communications are issued at the beginning of FDA's assessment prior to conclusive determination of the clinical or public health significance of the information under evaluation and before a decision has been made about what regulatory actions, if any, should be taken. All of our communications are available on our Web site, disseminated through our MedWatch Partners Program and our LISTSERV that includes 92,000 subscribers.

FDA plays a critical role not only in the detection and management of safety issues, but a critical role in communicating this information to the public. Our goal, regardless of the tool that we use, is to make the most up-to-date drug safety information available to the public in a timely manner so that healthcare professionals and patients can consider the information when making decisions about medical treatment. We are committed to providing accurate, clear, reliable and useful drug safety information to the American public.

Thank you for the opportunity to testify and for being before the Committee today. And again, we are happy to respond to any questions.

[The prepared statement of Dr. Seligman appears on p. 101.]

The CHAIRMAN. Thank you for your testimony. You know, the reason why we put you on panel two instead of panel one is so you could hear the testimony of panel one. It looked like you were listening attentively, but your testimony made no reference to it. I understand the process and on paper it looks fine. We had testi-

mony—I agree it is one individual—that said this process didn't work. You both spent your whole time saying it depends on informing the health professional. Well, you don't know that the health professional is informed. You send out something. We had testimony that it didn't work. The health provider didn't pass on those warnings. There was no consent form that was ever offered. He came and reported emergency problems, which were dismissed. So all that data that you have depends on someone reporting it. What if we have every health professional treating their patient like Mr. Elliott? If that happened, your data is useless.

So we have a reality. That is why we had panel one. The process that you laid out did not work. I mean, is that what you heard or not?

Secretary PEAKE. Mr. Chairman, I did hear that and I truly had some difficulty following totally kind of the sequence of events there. But as you all asked your questions, I thought I understood where Mr. Elliott was in his experience. It sounded to me that he was treated for his PTSD, it was begun some time ago. He clearly had a problem with tobacco that was in fact considered by his healthcare professionals to be a problem and he wanted to stop smoking. And that was the criteria for being in this. It was also that you had relatively stable PTSD, not with other psychoses or serious mental illnesses or so forth. When he started on the medicine by his private physician, by his personal physician, what was known and before any warnings came out from FDA, the early communiqué—even before the early communication what was known was some of these dehydration——

The CHAIRMAN. Before the FDA warning, the doctors in the VA knew that there was something going on because they started their own internal review before that.

Secretary PEAKE. You are right. We start following——

The CHAIRMAN. You knew something——

Secretary PEAKE [continuing]. The post-marketing survey in conjunction with working with the FDA.

The CHAIRMAN. So people knew something before the November incident. Why was it never communicated to Mr. Elliott's physician?

Secretary PEAKE. Sir, there was very little information to make any qualified judgment about this medication. As I indicated, it was like half of 1 percent that we were getting some reports on.

The CHAIRMAN. Based on the information——

Secretary PEAKE. That information was shared with the FDA to say "what—are you seeing anything?" I mean, it was one of the things that was discussed with the FDA. I agree that—with Dr. Seligman, that they really are the gold standard and we——

The CHAIRMAN. But you heard testimony that the process broke down. Neither the information that the health provider should have passed on nor the symptoms that the patient had were included in your data. Doesn't that give you some pause about your incredible confidence in this gold standard system? It depends on these individuals having that same——

Secretary PEAKE. Sir, you are right.

The CHAIRMAN. Is this doctor going to be asked about this testimony, for example?

Secretary PEAKE. I beg your pardon, sir?

The CHAIRMAN. Is the doctor who Mr. Elliott said did not inform him of the side effects going to be questioned about that?

Secretary PEAKE. Yes, sir.

The CHAIRMAN. Thank you.

Secretary PEAKE. I would like to also make it clear that——

The CHAIRMAN. Is the process we are going to be looking at in other VA facilities where people did not take seriously the emergency status of the individual leading to suicides in other cases—almost suicide in this case—is that going to be looked at in the detail that Mr. Walz talked about?

Secretary PEAKE. It absolutely will, sir. In this particular case as well. And I will tell you I totally agree with your concern about suicide as an issue. As we talked last night, we are continuing to address that as a significant issue, one that we need to be very concerned about. I will tell you that there is great literature to support the notion that smoking itself, ongoing current smoking itself is associated with suicidal behavior. So, you know, this is a very complicated subject.

The CHAIRMAN. Of course it is.

Secretary PEAKE. Smoking is a bad problem and it kills people.

The CHAIRMAN. So does suicide.

Secretary PEAKE. I agree.

The CHAIRMAN. What disturbed me in the press accounts leading up to this hearing was Dr. McFall was quoted as saying there is no causation here, we'll wait until the study is over. Well, if there was causation, we would know because some would be dead.

But it seemed to me that you had a limited number of people, something like 144, that were particularly fragile because of PTSD. It was a small group of people. You could have called them all. I mean, if it was my child involved, I would have wished that you would have called them all. They had 144. Call them, tell them what is going on, tell them to come and visit the physician. Deal with these people in a very personal way. You are dealing with everything bureaucratically. You issue a letter to 225,000 people, you think it is going to be read by everybody, you think everybody is going to follow it, you think the patient is going to be heard. Call the patients. You have their phone numbers. Call them up. Tell them they have PTSD, they are taking Chantix®, they need to see their physician immediately.

As Colonel Charles said, there is a higher bar in this kind of study. There is a higher bar and I don't believe you met it and you could have. I mean if you had asked me, as soon as I read it, I would have called 144 of them and gotten them in to the doctor. But now, we are going to wait until the study proceeds because it is only .1 percent; we will take 4 months to study this and on and on and on. This is life and death. And you are operating as a bureaucracy, which takes months and months and months, and we saw possibly only one of the outcomes.

You found others that bother me particularly. I don't care if it is 1 percent or 50 percent. From the testimony I will bet that you don't know all the data.

Secretary PEAKE. Sir, I will tell you that I would have—I was—we had about 240—there were 945 people in the study, on both

arms of the study, and only about 241 of them were taking Chantix® any time during that study. One of the reasons I have asked for a detailed review of this study, in particular, is to understand where we might have fallen down in terms of the notification. We have only about half of the folks that have signed——

The CHAIRMAN. But you are still studying it and there are still people in it. I would have suspended the study until you found out if there is causation. You have 40 people left. Get them off of the drugs. Don't take any chances.

Secretary PEAKE. Forty people smoke and are trying not to kill themselves with smoking. And I think it is up to the doctor and not an editor or not perhaps a Committee that ought to withhold a medicine from a doctor.

The CHAIRMAN. If the doctor didn't do his job, we are in trouble.

Mr. BUYER. Mr. Secretary, you have had over 40 years in the United States Army in many capacities, but most of which as a medical doctor, sir. I almost had a flashback here that I was back at Fort Eustis as an Army Judge Advocate General captain sitting in to give legal counsel to the Quality Assurance Risk Management Committee that was examining whether a particular doctor exercised good judgment in the interest of their patient on whether or not it gave them the proper consent about the advisory of a drug. And in this particular case, I look at this one as a layperson and we have an individual who was taking a particular drug that Mr. Stearns had had an interaction with this individual and the drug had a neuropsychotic side effect; i.e., suicide ideation. So he is already taking that drug and now all of a sudden he is prescribed Chantix® and then when the doctor learns that there is an advisory opinion on Chantix® that also could have a side effect; i.e., suicide ideation, now I have a patient that is taking two drugs that have a possible side effect of ideation. What are the propensities or the multiplier effect of that, of the interaction of both of these drugs, on top of that taking alcohol?

I mean, that is pretty volatile, I would think. And so I kind of look at this and say, okay, we have a large VA study and you have many institutional review boards. About how many do you have?

Secretary PEAKE. Sir, in this study there were 10. There were 11. One was the oversight where they weren't treating patients. So really 10 study sites.

Mr. BUYER. And are the 10—but outside of this study, you have about 100—are there about 120 institutional review boards?

Secretary PEAKE. One-hundred seventeen, sir.

Mr. BUYER. There are 117. But 10 of those participated in this study?

Secretary PEAKE. That is correct.

Mr. BUYER. And do each of these institutional review boards sort of act independently of each other?

Secretary PEAKE. In fact they do. That is their charter, to ensure that at that institution, that the medicine and the science and the protection of the human subject is paramount.

Mr. BUYER. So we boil this down quickly; when the Chairman sort of gave us a charge in his opening about how are the execution of procedures, I look at this and say, well, first what is so important is the doctor/patient relationship, the doctor having the best

of the interest of his patient at heart. And that there are many drugs out there, there are many advisory opinions that come down and they are to keep their patient's best interest at heart.

Now, we have a case whereby—the testimony of Mr. Elliott, whereby he said he didn't sign an addendum to an informed consent. My question is, just because there is an advisory opinion by the FDA, does that mean that there is required to be a signed addendum to an informed consent?

Secretary PEAKE. There is not, sir. The reason that we provided the addendum was in the very first consultation where he said he had 3 hours of counseling to understand this study and seemed to understand it pretty well. In that environment, he was told that we would inform him if there was any changes in the treatment for smoking cessation. And so that was our obligation, to make sure that we informed all of the folks in this study about the change.

Mr. BUYER. So we have 10 institutional review boards, each acting a little bit different with regard to the advisory opinions. As of now, no black box advisory from Chantix®. Chantix® is still a legally prescribed drug, correct?

Dr. SELIGMAN. That is correct.

Mr. BUYER. And, Dr. Seligman, is it accurate or fair at all for me to describe Chantix® as a suicide inducing drug?

Dr. TEMPLE. No, I don't think we know that. What we have is evidence, but it is not really complete. It comes from spontaneous reports that there are people who became suicidal on the drug.

Mr. BUYER. I don't need the clinical. It is not accurate to call it a suicide inducing drug?

Dr. TEMPLE. Not that we——

Mr. BUYER. The last comment—thank you, Mr. Chairman—is, Mr. Secretary, with regard to your interest on the pharmacological protections and surveillance, you have some findings from the Data Safety Board. Could you advise us to that? Was there any review from a Data Safety Board?

Secretary PEAKE. Yes, sir. Our Data Monitoring Committee. Sorry, we changed the name and I am catching up with the name. In fact, they reviewed all of the data, all of the SAEs, and basically said that they found no reason to alter the study, that they found no reason to withdraw the use of any medicine in the study and that they concurred with all of the steps that had been taken and in the way that they had been done.

Mr. BUYER. Could you provide that to the Committee?

Secretary PEAKE. I can, sir.

[The following information from the VA was subsequently received:]

Question: Can you please provide the Data Monitoring Committee's review of adverse events and serious adverse events?

Response: The Data Safety Monitoring Board (later renamed the Data Monitoring Committee) met in both open and closed sessions on February 27, 2008, to discuss several issues related to Cooperative Studies Program (CSP) study #519 on smoking cessation. During the open session, one of the principal investigators raised questions about the high number of serious adverse events and the Committee agreed to collect adverse events and serious adverse events, which would be reported to the Food and Drug Administration together. The Committee further analyzed data on serious adverse events while in closed session.

The Data Monitoring Committee reconvened on July 3, 2008, where the members discussed the incidence of serious adverse events in both closed and open session.

The attached minutes from the Data Monitoring Committee meetings held on February 27 and July 3, 2008, included portions which were closed sessions. This information must be withheld from the investigators so as to avoid biasing their research and will not become part of the public record. The minutes are being retained in the Committee files.

Mr. BUYER. All right. Thank you, sir.

The CHAIRMAN. Thank you.

Mr. Hare.

Mr. HARE. Thank you, Mr. Chairman. Mr. Secretary, welcome to the hearing. I did not read *The Washington Times* article, but coming out it said that it took the VA 3 months to notify veterans of the side effects of the Chantix® and that the warning letter was tied up in "bureaucracy," according to the article.

Would you care to respond to that? And then if so, why did it take so long and do you think that is an appropriate time frame?

And then lastly, what do you think we need to do to make the bureaucracy more efficient so our veterans are timely and appropriately notified?

Secretary PEAKE. Sir, first on the timing. The 3 months I think came from the idea that on the 20th of November the early communication came out. In fact, the very next day we notified the clinicians through our pharmacy benefits channel. There was not felt to be, and I think appropriately so on the basis of that very early communication, a reason to go out and contact every patient that was on Varenicline. I don't think that was—I think that was an appropriate judgment at the time.

The other aspect of it, sir, is on February 1st, when the public health advisory came out from the FDA, that was a more—we took that more seriously in terms of as a call to action, if you will. Again, immediately that was passed both through research channels and through our clinical channels to those that prescribed Chantix® and had patients on Chantix®. In the mid month, the research community that was responsible for the study got together and had a discussion about it and decided we should notify our patients, and that is when that letter that I described was put together, along with the addendum that was put together for the consent, and that was sent to each of those review boards that I talked about, the 10 review boards that the Ranking Member mentioned. Each of them then had to decide what is the best way to notify the patients locally and should they do it and did they want to change? One review board rewrote the letter, kept the same tone and everything, but went through that deliberation because they felt that is their responsibility. And so there was a lapse. Some, Washington Hospital Center as an example, sent that letter out by the end of February. So that would have been a one-month delay, if you will, or perhaps an appropriate deliberation period. Others didn't send it out until June. That to me, I am not sure I understand why, that is why I have asked Dr. Puglisi to take a good look at all these and understand why.

I think we have—going to your next question, sir, the problem is that we do have all of these independent review boards when we are doing cooperative studies and I think—and we are already

starting a central IRB, Institutional Review Board, so that we can have better and tighter discipline in terms of the execution in a study like this so they have a common standard, so everybody is—you have a way to hold people accountable, to be able to get the word out.

The other piece is we will be looking, as part of our deep dive into this particular environment, to understand what kind of—going back to the Chairman's point, what should we be doing if we want to notify a patient? Do we need to call them? Do we need to send by return mail? So that we have a standard as opposed to do-it-however-you-feel sort of best at the local level.

So we will be instilling that kind of discipline as we move through our system and move through our review of this particular case and apply it across the VA.

Mr. HARE. I would appreciate that, Mr. Secretary. I appreciate your willingness to look into the situation with Mr. Elliott, and I also appreciate you being here today. And with that, Mr. Chairman, I yield back.

The CHAIRMAN. Thank you, Mr. Hare.

Mr. Stearns.

Mr. STEARNS. Thank you, Mr. Chairman. Let me welcome the Secretary of Veterans Affairs. How long, Mr. Secretary, have you been in this position?

Secretary PEAKE. About six and one half months, sir.

Mr. STEARNS. Six and a half months. Okay. And I was just reading your distinguished biographical data on you, that you are a retired lieutenant general, you went to West Point and that you also served with distinction in Vietnam and you got the Bronze Star with a V, the Silver Star, Purple Heart, Oak Leaf Cluster. So you have served your country admirably and we appreciate your service and we also appreciate you willing to take on this very difficult job of being Secretary of Veterans Affairs.

I think I will just get to maybe a very important point that we should all establish here. Do you have the numbers that we could know today for veterans who have participated in the smoking cessation program who have actually stopped smoking; for example, using the nicotine patch, how many have actually stopped, using the nicotine gum, and then Chantix®? Has there been any data that we know of that you could give us today?

Secretary PEAKE. Sir, this has—this is a long-term study. It is not over yet. We don't have it all closed. But the principal investigator is here and perhaps has some insights into that.

Mr. MCFALL. Thank you for the question. The study is due to be completed in July of 2009, meaning all of the enrollees, the participants, will have had their follow-up data then. At that point would be the appropriate time for us to be able to give the analysis to you and then the study will essentially——

Mr. STEARNS. Give me a premature blush; that is, is the smoking cessation program working?

Mr. MCFALL. The biostatistician has that data. I do not. I am a principal investigator and I am deliberately kept blind to that data so as not to bias——

Mr. STEARNS. So you can't tell me if the nicotine patch or the nicotine gum is working at all?

Mr. MCFALL. I am not personally able to do that because I do not have access to the data. I am kept blind. They don't want me to see the data for fear of biasing the outcome. The only persons who really know that are the study biostatisticians.

[The following information was subsequently provided by the VA:]

Preliminary Results of the Study

Question: Do we have any indication of the results of the study? Can the study's biostatisticians provide any data to the Committee?

Response: The Department of Veterans Affairs cannot release any results of the study until its completion in July 2009 so that we can preserve the data's integrity and the study's validity. However, information about adverse events is submitted for review to local Institutional Review Boards, Human Rights Committees and the Data Monitoring Committees to evaluate whether there is a clear harm or benefits for participants while a clinical trial is still ongoing. VA shared this preliminary information in testimony before the Committee on July 9.

The study in question is not a drug trial of varenicline, and is not designed to provide information on the safety and effectiveness of varenicline, bupropion or nicotine replacement therapy. The study is seeking to determine if it is easier to stop smoking when smoking cessation treatment is combined with PTSD therapy, or whether the two therapies are more effective if they are provided separately. In this study, patients may be receiving one of several proven smoking cessation treatment options, including counseling, behavioral modification and/or drugs prescribed by their own physicians. Drugs include varenicline, bupropion, transdermal nicotine patches and nicotine gum, all of which are on the VA Formulary and are Food and Drug Administration (FDA) approved treatments which have undergone substantial evaluation to receive FDA approval. "The Medical Letter on Drugs and Therapeutics" has found, based on their evaluation, that ". . . varenicline is the most effective drug available for this indication (smoking cessation), more effective than nicotine replacement therapy or buproprion SR (Zyban)."

The study chair is kept "blind" (unaware) of the results until all data have been collected and analyzed. "Blinding" is an important means for reducing or minimizing the risk of biased study outcomes. This commonly used mechanism in clinical trials research helps to prevent preliminary results from influencing how the study is conducted or other key study decisions. However, results of the study ("unblinded data"), including adverse events and serious adverse events, are continuously monitored by other members of the study team, including the study biostatistician and study pharmacist.

Mr. STEARNS. There is no feedback then? I mean, this program has been going on since 2006, right? 2004. Almost 4 years and we have no data to indicate whether any of these programs are working?

Mr. MCFALL. The data is available. It is reviewed by the Data Safety Monitoring——

Mr. STEARNS. Oh, I know bureaucratically. I understand that. But you are here today to tell us these programs are important and you want to continue them. I am asking you, does nicotine gum work?

Mr. MCFALL. Well, the intervention is again, sir, not just about gum or patch or any other medication. It is a comprehensive program that includes counseling and medicines as optional.

Mr. STEARNS. Mr. Secretary, could you say as lieutenant general, if your superior said to you, gee whiz, General, we've had this program for almost 4 years, is it working, I want to know whether to continue it. What would be your answer?

Secretary PEAKE. Sir, what I would tell you is that the modalities that we are using are proven modalities for stopping smoking. The question to be answered that you can't answer in the short term is, is it better to do it with PTSD treatment or is it better to do your PTSD treatment separately from the smoking cessation environment. And that is why we are trying to answer this question. The modalities are proven modalities.

Mr. STEARNS. Let me ask you this, Mr. Secretary. I need you to elaborate. Of the 945 veterans who enrolled in this study, and I guess there are 245 on Chantix®. Were they counseled on the complications of this drug? Let me just establish that. Yes or no, were they counseled on the FDA clinical advisory of February 2008? Were they, yes or no? And I think the answer for you is you don't know.

Secretary PEAKE. Well, I will tell you that each of them——

Mr. STEARNS. Because it is on your watch. February 2008, FDA made this advisory——

Secretary PEAKE. If your question is were they counseled specifically about the FDA warning, I cannot definitively tell you that at this point.

Mr. STEARNS. So the answer would be no. Now, when I go through and I go to Hampton, Virginia, and I see the number of people who are taking Chantix® and the people who had a consent agreement—and I saw the consent agreement—what it looks like. Out of the 28, 15 had no consent agreement. Then I go to Houston, Texas. Of the 35 there, 19 there was no proof of consent agreement. When I go to Minneapolis, there is 14 out of——

Secretary PEAKE. About 50 percent of them don't have——

Mr. STEARNS. What I am saying, Mr. Secretary, in all deference to you, here is a program in which you are not getting consent agreement from the patients. And that seems to me a bad procedure and that somebody should have taken care of it because you should get consent agreements—in the 3 hours of counseling that was done for these folks in the beginning, there wasn't any kind of counseling done for Chantix® or any kind of advisory after the FDA issued this in February of 2008; is that correct?

Secretary PEAKE. Sort of. Let me explain it if I may. Chantix® was not added to the study at all until it became FDA approved and then put onto the addendum that was created at that time based on what we knew about Chantix® at that time. As the FDA has testified, there is emerging information that goes along with it.

Mr. STEARNS. I will grant you that point. But I gave you Houston, Minneapolis, Hampton, Virginia? I mean, 50 percent of these people are not getting any consent agreement. Don't you admit that is wrong?

Secretary PEAKE. First of all you need—the consent agreement is really an addendum to the consent form. They already agreed to the study.

Mr. STEARNS. Shouldn't they get an addendum to the consent form?

Secretary PEAKE. The addendum to the consent form is to ensure that they have been informed about the change. The answer is yes.

Mr. STEARNS. No. The question is should they have an addendum to the consent form? Yes or no.

Secretary PEAKE. Yes.

Mr. STEARNS. They were not done here.

Secretary PEAKE. They were sent the addendum in the mail.

Mr. STEARNS. Why were 50 percent of these not signed and you couldn't produce them?

Secretary PEAKE. Part of the reason is because they were—said if you are doing fine, come in at your next visit, which could be 6 months later, and we will sit down and go over it. But you have the information in hand. So that is part of it. Part of it is—I am concerned—some people moved out of the area——

Mr. STEARNS. Have you taken procedures to correct this so that if I come back in 6 months and I pull the same data, it won't be that 50 percent have not signed the addendum to the consent agreement? Have you taken procedures to do something about that?

Secretary PEAKE. That is exactly what this in-depth study of this particular——

Mr. STEARNS. Do you need a study to get conformance on a consent agreement addendum?

Secretary PEAKE. What I want to do is make sure we have the right processes and we can be able to hold the accountability right down to the grassroots level to ensure that these kinds of things, to include this consent agreement, get done.

Mr. STEARNS. In all fairness, if you were chief executive officer of a company and I saw this data, I would call up Houston, I would call Minneapolis, I would call Hampton and I would get together on the phone and say get the addendum consent agreement right now.

Secretary PEAKE. That has been done.

Mr. STEARNS. You have done that?

Secretary PEAKE. That has been done.

Mr. STEARNS. Okay. Okay. All right. Thank you, Mr. Chairman.

The CHAIRMAN. Thank you, Mr. Stearns.

Ms. Berkley.

Ms. BERKLEY. I thank you, Mr. Chairman. This has been perplexing to me. Could you, Mr. Secretary, explain to me, was this gentleman, Mr. Elliott, part of the study, not part of the study, and if he was part of a study, what were we studying?

Secretary PEAKE. Yes, ma'am. He was part of the study. The study was to see if it is better to get smoking cessation treatment, whatever that may be between you and your doctor, whether it is counseling alone, whether it is nicotine patches, whether it is Chantix®—whatever you and your doctor decide is the best smoking treatment for you; if it is better to get that treatment from the guy or gal that is giving you your PTSD treatment, or get your PTSD treatment separately and smoking in a different environment, smoking cessation clinic or your primary care doctor or whatever.

Ms. BERKLEY. How long has that study been going on?

Secretary PEAKE. It has been since 2004 and it should be concluded here in 2009. And the idea was not just can you stop smoking this week, but what is your long-term ability to stop smoking? Because that is really ultimately what makes a difference for people's health and life and complications of smoking.

Ms. BERKLEY. So it is essentially if you have PTSD and you are a chronic smoker how do we best treat both of these symptoms, or both of these problems I should say?

Secretary PEAKE. What is the best place to do that treatment, is it better to get it from your PTSD doctor. PTSD people smoke more than twice the rate of other people. So it is a big problem for them.

Ms. BERKLEY. Let me ask you something and I hate to call this woman the lady doctor, but I don't have her name in front of me. My stepdaughter is a lady doctor. I think she would be very offended if I called her that. Was she part of our VA? Was she a VA doctor?

Secretary PEAKE. Yes, ma'am. In fact, yes.

Ms. BERKLEY. So she was treating Mr. Elliott for his PTSD symptoms—problems and his smoking?

Secretary PEAKE. Yes, ma'am. You know, he has not released his medical records, so I really can't get into the discussion about his—the details of his healthcare.

Ms. BERKLEY. I am kind of gleaning from his testimony that she was his psychiatrist and she had recommended to him that he take this anti-smoking medication, that——

Secretary PEAKE. From his testimony, that is what I gather. In fact, it sounds like others have talked to him about the smoking problem before.

Ms. BERKLEY. So he signed his consent form that had patch and had gum but did not mention this other drug but he consented to it, obviously he started taking it on the recommendation or suggestion of his doctor. Did the information on the adverse effects of the drug get to his healthcare provider, his psychiatrist? Was she aware of it?

Secretary PEAKE. She—the procedure was in place that she should have been aware of it. I do not know.

Ms. BERKLEY. Is the breakdown—I am sorry. I don't mean to step on your answer.

Secretary PEAKE. No. I actually think that she would have been aware of this. And through all of the things that we have already talked about in the manner in which we communicate down to the physician.

Ms. BERKLEY. Okay. So we are going to assume that she had the alert but we do not know and, according to Mr. Elliott's testimony, she did not communicate the potential adverse effects to her patient, to the VA patient?

Secretary PEAKE. That is—I agree with you, that is what he said.

Ms. BERKLEY. Now, are you developing protocols to ensure that this information gets to the patient? Now he may have decided on his own not to take it, he was beginning to have a lot of adverse symptoms, but he was not informed, I guess, officially, according to his testimony, that there were possible psychotic problems.

Secretary PEAKE. Right. We should make it clear about the timing of this. The FDA alert came out on the 1st.

Ms. BERKLEY. Right.

Ms. BERKLEY. And he was also breaking out in rashes and other things.

Secretary PEAKE. As I believe he testified, he did see his doctor and talked about the rashes, and so forth. So they were aware of

that. I think the real question is was he counseled about what we knew at the time about potential psychological issues.

Ms. BERKLEY. How do we find that answer out?

Secretary PEAKE. It would have to be with inspecting the medical record.

Ms. BERKLEY. All right. When he came in for emergency help—and I think this is something that concerns us all, where was—why——

Secretary PEAKE. It concerns me and I actually don't know. I will find out.

Ms. BERKLEY. Has anyone been in communication with the lady doctor?

Secretary PEAKE. Ma'am, I have not heard that—his emergency problem and not having care until he testified here today.

Ms. BERKLEY. Because it sounded as if he knew he was having a meltdown, he did what appeared to be the appropriate thing; he went back to his psychiatrist and was asking for immediate intervention and did not get it?

Secretary PEAKE. That is what he testified to. As I say, that is something we need to drive down and make sure what really happened and ensure that it would never happen again.

Ms. BERKLEY. Let me ask you another question. How does the VA monitor the number of medications that are being taken by our patients? And as you know, I had the Justin Bailey situation in my district where he was taking multiple medications and was prescribed yet another and died of an overdose. And the combinations—it would seem to me knowing what Prozac can do, exacerbated by this anti-smoking drug that seems to have the same issues, plus a couple of glasses of beer, I mean, that seems like a real problem. Is anybody—forget the beer—how do we monitor, if you are taking Prozac and now you are being prescribed this, this should be a red flag.

Secretary PEAKE. It should be something that your provider really understands and is making a conscious decision based on you and your care. In this particular case, my understanding is that it would have been the same provider making both the prescriptions from what I heard him say. Now, I would also tell you that with our computerized patient record, it gives us an advantage over other places because there is an opportunity for medicines reconciliation where you see all the medicines that that person is on unless they get them from outside the VA or something. But all the medicines that are prescribed so that the provider can have that information readily at hand to try to make those decisions.

I will tell you also that I do agree that we are concerned about this issue of polypharmacy and we have asked specifically, our Pharmacy Benefits Management Group to take a look using our computerized system—to see how many people really are on multiple—the same kinds of multiple classes of drugs and so forth. So I am looking forward to getting the information back from them so we can do a better analysis of just that problem, not necessarily related to this study, but it would include looking at these same medications, though.

Ms. BERKLEY. And also is there a way that we monitor—and I don't want to accuse—my husband is a doctor. I am not accusing

anybody. But do we know the quality of our doctors? Perhaps there was an individual doctor that was at fault here? Is this a problem systemwide with the VA? I mean, how do we get to—how do we solve this problem and what can we do in the future? And when will you be reporting back to us the information that you are going to gather?

Secretary PEAKE. I would be delighted to report back to you the information we find out about this case. Very quickly because we will get to it quickly. However, I will tell you that we have the same kind of credentialing process, the same kind of peer review, the same—many of our doctors are affiliated with medical schools and universities, and so I think we have quite a high caliber of medical professionals throughout the VA and I think it is—so you have to rely on some level on their professional qualifications and judgments.

Ms. BERKLEY. I don't doubt the level of expertise of our VA doctors. I am just concerned that we had a breakdown here and how do we prevent this from happening again?

Secretary PEAKE. And I am concerned about the same thing, ma'am.

Ms. BERKLEY. And when do you think you will be getting back to us with a report on what transpired in this particular case and how we are going to be able to prevent this in the future?

Secretary PEAKE. I will shoot for the end of next week. How about that?

Ms. BERKLEY. That is impressive. All right. Thank you very much.

[The letter from VA appears on p. 129. The attached report will be retained in the Committee files due to confidential personal information included in the report.]

The CHAIRMAN. Don't shoot anybody.

Mr. McNerney?

Mr. MCNERNEY. Thank you, Mr. Chairman. Secretary Peake, thank you for coming and testifying today. Like I said to Mr. Elliott, I am sure this isn't an easy hearing for you. I believe there are two important issues here. The first is should risky treatments be administered to vets, especially vets suffering from PTSD, and second, if so, are they being administered under sufficiently careful conditions that includes letting the vets know that there is a risk involved? Especially this kind of risk. And is that information being disclosed as soon as possible?

As Mr. Buyer pointed out, a professional should probably decide the first question, but the second question in my opinion is clearly under our jurisdiction. It appears that warnings were not being passed along and we want to make sure that appropriate procedures and responsibilities are in place to prevent this from happening again.

Let's recap what happened here. On November 20th, the FDA notified the VA of serious side effects. On February 29th, participants using Chantix® were notified. Why did it take so long? That is the basic question.

Secretary PEAKE. Well, sir, I would tell you that that early warning was absolutely considered by healthcare professionals and even by, I think, the discussion by the FDA here, it does not rise to the

level where alarming or reaching out to try to touch everybody on the medication. We did not do that. I don't think anybody did that because I don't think it was the appropriate standard of medical practice to do it.

Mr. MCNERNEY. That is a matter of judgment, then.

Secretary PEAKE. It is a matter of judgment, sir. That is my point. It is a matter of judgment that healthcare professionals considered seriously and felt it was not—you know, not warranted. So I agree with you, it is a matter of judgment.

And I guess I would say, going back to Ms. Berkley's point, we really have some very high quality people who are used to taking care of patients with PTSD, who are used to using these medications that were part of that consideration.

Mr. MCNERNEY. Well, in conjunction with that, VA doctors, according to the *Times* article, *The Washington Times*, the VA doctors were reporting concerns about Chantix® causing serious events throughout 2007. Was this information acted upon in any way?

Secretary PEAKE. Yes, sir, it was. In fact in—I think it was about October of 2007, as I say, we had seen half of 1 percent of folks on Chantix® have something. Whether it is related to Chantix® or not, you can't really tell. We are still not clear. And I don't think FDA has made a causal connection with these issues and Chantix® either at this point. But that information, along with some anecdotal stuff, hey, Joe, I am seeing this, are you? And that information was passed to FDA because we have a member on the Safety Board there to say let's take a look at this and because we don't have—and there was, I think, already mentioned about 7 million patients on Chantix®—the VA has had about 70,000 and we haven't seen a big blip in, you know, over the course of treatment. It is about a 12-week treatment that can be extended to 24 weeks. So it has a longtime exposure. And so I guess I would tell you there was action taken. We were looking at it all along, starting in—I guess it was October we started adding the things we were watching more carefully to try to understand if there were more serious—or psychological side effects, adding to the data.

That is what led to that discussion in December, that review in December that I discussed in my opening statement. So that we started looking at really in more detail to try to understand is there really something here that we ought to be more worried about. So, the notion that we weren't doing anything I think is not correct.

I appreciate the Chairman's point, that if you were a dad, would you want—but, as we talked last night, I said if I were you sitting down with your doctor, do you want them not to have what is said to be the best medicine to help you stop smoking if you are a two and three pack a day smoker?

Mr. MCNERNEY. Right. But you also want to tell them that there is a risk involved.

Secretary PEAKE. Yes, sir. On the 20th of November, that first notice came out. On the 21st of November, we passed that through the clinical channels so all the clinical people would have that information available to them.

Mr. MCNERNEY. Well, in my experience, this Committee has been finding out about serious issues from the media rather than

from the Veterans Administration itself. *The Washington Times* report is an example. Do we have a lack of accountability here? Is that why we are not hearing—why aren't we hearing it here in the Committee before the newspaper tells us?

Secretary PEAKE. You know, sir, with all due respect to the newspaper, as I have testified, I think in this case, except for the issue of the execution in the particular study of the signing of the consent addendums and doing that promptly and so forth, I think the clinical decisions have been appropriate and, you know, it is always tragic and I tell you I have absolute sympathy for a fellow CIB wearer that has had those kinds of problems and had the trials and tribulations of PTSD and so forth. I mean there is no—absolutely I am sympathetic to a fellow soldier. But, to say, well, should we act on that single case and deprive the 32,000 people out there who want to stop smoking from being able to work with their doctor, to decide is this the right therapy for me with that doctor knowing—having the information—and as I say, we keep updating the information as we get it. If the FDA in conjunction with us or we see something that suggests that this ought to have a black box warning or be a recall, I mean, we can do that very quickly and we would. And without hesitation I would restrict it within the VA if the evidence started to show that this was something that was truly putting our veterans at risk.

Mr. MCNERNEY. Well, I think the VA has some excellent policies in place to safeguard the veterans. My concern is, are those safeguards being followed? Are the policies of the Veterans Administration being administered properly in the VA?

Secretary PEAKE. Sure, that's exactly why I have asked for these particular internal reviews of not only this study, but other studies as well, to also look specifically at our pharmacy program and how we cascade information and how quickly we do it and the standards to which we hold people.

I agree with you.

Mr. MCNERNEY. Again, thank you for testifying; and I do look forward to working with you to resolving these problems that have come to light today.

Secretary PEAKE. Thank you.

Mr. MCNERNEY. I yield back.

The CHAIRMAN. Thank you.

Mr. Walz.

Mr. WALZ. Thank you, Mr. Chairman.

And, Mr. Secretary, thank you again for spending your morning down here. You have been very open since your tenure started just a short time ago in addressing these issues. I really appreciate that.

I also want to make notice of the focus on the quality of care and especially on the research and the preventive side that the VA is taking—what I think is almost a unique position in American healthcare in dealing with that. And you have been dealt some pretty heavy ones, especially smoking.

I know it's several decades ago, but when I ended up at Fort Benning, the 60 in my platoon, 5 of us didn't smoke. So, very common amongst members who have been there, so—and, rightfully,

the causation between that and everything else that comes out of smoking is a focus.

Now, we also agree that PTSD falls into a psychological disorder that can cause problems, too, down the road. It's on a spectrum, I am assuming, from mild to severe. So the VA is dealing with two issues at the same time amongst veterans. And I understand that that's where the physicians and the medical professionals make a diagnosis on this.

And I am glad to hear—one of my questions was, how were you dealing with this or why are you dealing with that? You gave me data to say that these people smoke almost twice as much, on a much higher frequency, and things like that. So I am sure you are assuming and realizing that getting them off smoking—that you are trying to find out, does that help their PTSD recovery; is that correct?

Secretary PEAKE. Sure.

It's not just that it helps their PTSD recovery. We—smoking alone is a reason to stop. I mean, it has——

Mr. WALZ. Do we know that smoking is not a release from the tensions of PTSD? I mean, I don't like to think that's a positive thing. I mean, it's a lesser of two evils, but that has to be a consideration, correct?

Secretary PEAKE. It is. And actually one of the secondary objectives of the study——

Mr. WALZ. That's why you picked stable PTSD?

Secretary PEAKE. Yes.

Mr. WALZ. Now my question comes up now—and this is where perception becomes a problem. When I heard the testimony of Mr. Elliott, it seemed that at first there was more of an emphasis on getting him in a smoking program than dealing with the PTSD on the first, initial consultation.

And, again, perception is a problem. This is where we have to talk to the public. It is the gorilla in this room, as we speak about your predecessor's relationship with Pfizer, the maker of this drug, which brings up concerns.

Now, whether those are founded or not is something we have to ask. So now we are in a situation where a soldier comes in with PTSD, his first consultation is to get into a smoking cessation program, which I applaud grandly. This is a great initiative, it's one that nobody is probably doing better. And I agree that if this drug can be proven to be safe, and take out the drug interactions and all of that, I want to see it work for people and get them off of this.

My concern is this part of it that appears—that's where I think the questions come up. So I think the things that are in place from the procedures that Mr. Buyer initiated with some of the oversight to the IG—I would ask you, Mr. Secretary, what was the most troubling about the IG report to you? I mean, what did you find most troubling about this whole situation?

Secretary PEAKE. What really troubled me about the IG report was, when they went in—and they went in quickly, and I thought they did a good job, but they seemed to have difficulty at the Washington VA of getting the information that was, how many people do you really have on this? Okay.

Well, that was a question that was raised in the IG report, and why that couldn't be answered right away concerned me. The idea that they couldn't find the consent forms easily, the fact that the second—the consent addendums had not been signed.

Mr. WALZ. That was exactly the part that I picked out, too, for two reasons. One is—and it's not a cover-your-butt situation, I know that; I know you better than that—that you want to get these to make sure that the veteran knows what they're doing, not after the fact to cover that.

My concern is the validity of the research then, the validity of the research—who is on it, when they have been taking it. And in some cases, they couldn't provide that. They couldn't say who was getting it.

So now, as Mr. Stearns pointed out, we are 4 years into this study. And if we have an issue of validity and reliability, that's a concern.

Secretary PEAKE. Sir, I would like to clarify that. Because it really doesn't matter from the research perspective, because of the question that's been asked in this research, what drug they're on, or if the issue is, did they get their—at the end of the day, did more of them stop smoking if whatever they got was from their PTSD provider; or whatever they got was—from a smoking cessation perspective, was provided by a smoking clinic or their primary care doctor, it doesn't really matter which medicine that they are on.

That's sort of a byproduct of the fact that you are in a study, so you keep looking at those things.

One of the things, probably—we didn't—the other thing that concerned me, on the 18th of June, we had 143 people, I was told, had been on Chantix®. When I started rolling it back and seeing there were other people—had been on Chantix®, so we came up with a total of 241. That is because we were able to go and search our database that nobody else really has like that, and be able to say, okay, who got a prescription someplace else that was still in the study?

So, you know, to answer the research—from a research perspective it's not so important.

Mr. WALZ. Okay.

My last question—and I know my time is up, and I know this is much broader to ask you to deal with these issues in a green, yellow and red time zone here, it's tough—my concern is, and I hear this time and time again, is the mental health providers and the lack thereof in the system in general. That might be the bigger framework that we are dealing with.

Secretary PEAKE. Yes.

Mr. WALZ. My question to you is in the spirit of being proactive to solve this, what do we need to do there? How do we entice this? How do we make sure, like, these gentlemen sitting with you choose to go to the VA and not the private sector, especially mental health-wise?

After that, I will yield back.

Secretary PEAKE. Couple of points, sir.

First of all, we have really been on a hiring push. We are up to like 3,900 new mental health providers. Today, we have announced

an increase in our Vet Centers, 39 new Vet Centers, because that gets people in, because it's a nonstigma environment and, you know, it's very receptive and they do a lot of outreach.

So, you know, there's pieces there. As I mentioned, we are going to hire another 145 suicide prevention coordinators, more mental health people to put out there to be able to manage folks. And so, I think—I don't know, specifically, at Washington Hospital Center what the workload for this particular doctor was. That's part of the thing we will look into. I mean, there's no reason for somebody not to be able to access emergency care when they need it.

Mr. WALZ. If I could, Mr. Chairman, just on the record here, I would like to point out, the followup that was done on the incident in Minnesota was highly professional, was very detailed and got to the heart of what the situation there was. And that entire process through this step of the way, I was kept very well informed by them.

So I know Ms. Berkley is no longer here, but when the Secretary says he will follow up on these situations, I trust that will happen, because I have seen it in action. So I thank you for that.

Secretary PEAKE. Thank you, sir.

[The following information was subsequently received from the VA:]

Mental Health Caseloads at Washington, DC, VA Medical Center

Question: Is there any indication that mental health providers at the Washington, DC, VA Medical Center are carrying too great of caseloads to provide quality care to patients?

Response: At the request of Representative Walz and the Committee, the Department of Veterans Affairs has reviewed average caseloads for mental health providers at the Washington, DC, VA Medical Center (VAMC). Overall, 90 percent of veterans are seen within 14 days of their requested appointment, and emergency care is available to those in need.

For general mental healthcare (including psychiatry, psychology, mental health consultation, post-traumatic stress disorder [PTSD], substance use disorder, and other conditions), between October 1, 2007, and July 15, 2008, the Washington, DC, VAMC provided 142,459 encounters and scheduled 93,780 visits for 8,569 unique patients. This information is included in a table below for ease of reference.

In regard to mental health staffing, the Washington, DC, VAMC has 106.5 FTEE:

- 22 psychiatrists,
- 1 psychiatrist,
- 19 psychologists,
- 1 psychologist,
- 17 Addiction Therapists,
- 5 Psychology Technicians,
- 10 Vocational Rehabilitation Specialists,
- 27 Social Workers,
- 34 Registered Nurses,
- 4 Licensed Practical Nurses,
- 5 Nursing Assistants, and
- 3 Nurse Practitioners.

In regard to mental health staffing within Trauma Services, which includes PTSD treatment, the Washington, DC, VAMC has 26 FTEE, including:

- 2 psychiatrists,
- 6 psychologists,
- 1 Addiction Therapist,
- 2 Psychology Technicians,
- 1 Administrative Assistant,
- 3 Vocational Rehabilitation Specialists,

- 7 Social Workers,
- 2 Registered Nurses, and
- 2 Clinical Nurse Specialists.

The Washington, DC, VAMC is actively recruiting to fill four vacancies of the 26 FTEE listed above, and they expect to fill two of these positions by the end of September. Between the PTSD Clinical Team's individual appointments and the PTSD Clinical Team's group meetings, the Washington, DC, VAMC had 19,607 encounters and 18,384 visits from 2,705 unique patients between October 1, 2007, and July 15, 2008. This information is included in a table below for ease of reference.

Washington, DC, VA Medical Center Mental Health Workload Data
(October 1, 2007, through July 15, 2008)

Source: Washington, DC, VA Medical Center, Office of the Director

Washington, DC, VAMC	# of FTEE	Encounters	Visits	Unique Patients
General Mental Healthcare	106.5	142,459	93,780	8,569
PTSD Clinical Team*	26	19,607	18,384	2,705

* = Figures include both individual and group appointments.

Washington, DC, VA Medical Center's caseload figures are comparable with other facilities across the Nation. The data below compare the Washington, DC, VA Medical Center's caseload figures to the most recently available national data, from fiscal year (FY) 2007. The Washington, DC, PTSD Clinical Team had an average caseload for the PTSD Clinical Team of 122 veterans per FTEE, versus a national average of 118 veterans per FTEE.

Comparison of Washington, DC, VA Medical Center Mental Health Workload Data with National Averages
(Fiscal Year 2007: October 1, 2006, through September 30, 2007)

Sources: Northeast Program Evaluation Center, VA Connecticut Healthcare System, West Haven, CT; *National Mental Health Program Performance Monitoring System:* Fiscal Year 2007 Report; *The Long Journey Home XVI: Treatment of Post Traumatic Stress Disorder in the Department of Veterans Affairs:* Fiscal Year 2007 Service Delivery and Performance; Washington, DC VA Medical Center, Office of the Director.

	# of FTEE	Visits	Unique Patients	Patients per FTEE	Visits per Patient
Washington, DC, VAMC					
General Mental Healthcare	145.3	80,358	8,117	55.9	9.9
PTSD Clinical Team*	13.7	20,732	2,705	122.0	7.7
VHA National-All VAMCs					
General Mental Healthcare	26,324.9	10,665,839	984,842	37.4	10.8
Providers who deliver PTSD Specialty Care*	684.5	828,245	137,822	118.0	9.9

* = Figures include both individual and group appointments.

The CHAIRMAN. Thank you, Mr. Walz.
Brief questions from Mr. Buyer, and then I will conclude.

Mr. BUYER. Thank you.

The CHAIRMAN. I am sorry.

Mr. BUYER. Dr. Snyder.

The CHAIRMAN. He just walked in. Do you want to ask questions of the Secretary? You are next.

Mr. SNYDER. Thank you, Mr. Chairman.

Mr. Secretary, thank you and your team for being here today.

One of the unfortunate things that was said today, I think, was that somehow implying that research at the VA is a bad thing or should be eliminated. That would be absolutely tragic. I mean, never in my history have I heard that view expressed before, and it would just be heartbreaking if somehow the take-home was, we should not be doing research at the VA system.

A lot of us have been advocating for more funds for research, and I think that this Committee in a bipartisan manner, and the leadership—Mr. Buyer, Mr. Filner and Mr. Smith before that—have been really strong advocates of trying to get you all additional money.

Also the nature of the study: This is the kind of study that doesn't get funded over this long term very much. Now, why is that? Because there's not money to be made in this study. This is about delivery of products that are already on the market. And I am a family doctor; we talk about that. We need more primary care research, because you are talking about where is the best place to do the treatment?

Now, the treatment may be exactly the same, but is it best to incorporate it as part of a PTSD clinic—I think the idea probably is, maybe they are more likely to come back on a regular basis to their PTSD clinic; maybe they are more accepting of a PTSD network—or should it be part of their primary care operation?

This kind of research—this country needs more of this kind of research, because there's no—at the end of the game, it turns out that it's best that it's in the PTSD clinic, and now somebody can go out and patent that and make a lot of money. It's not that there's not that kind of incentive here.

This is about delivery of healthcare. And, in fact, the VA system may be one of the few systems that is going to be able to do that because nobody will have that kind of money to support the research. So I commend you for doing that kind of research.

The issue of how many—I think I was trying to watch this, and I was like most people running around here—how many Americans do we think have used this drug so far—not veterans, Americans?

Secretary PEAKE. It's about five million Americans, I think. Internationally, it's about seven million, as I understand, sir.

Mr. SNYDER. Now, how long is the average length that people take the medicine?

Secretary PEAKE. Twelve weeks is the standard, and then they can up it to 24 weeks if they're doing well and still need some help, is what I understand.

Mr. SNYDER. What would be your guess, Mr. Secretary, this is out of your area of knowledge of those, you say, five million Americans?

Secretary PEAKE. Uh-huh.

Mr. SNYDER. When this additional information started coming out, how many of the ones not in the VA system, do you think, were notified by their physicians or practitioners about these changes in the warnings?

Secretary PEAKE. I would think none were outreached to specifically. I would think that because of the FDA's work in being able to get to the primary care doctors—as a matter of fact, if they read the warning, they may well, in the interface with their patient, have that discussion.

Mr. SNYDER. And they come back the next time?

Secretary PEAKE. Yes, sir.

Mr. SNYDER. I also like—I mean, we all rely on pharmacists so much. I mean, I do that with my kids and wife. When you get the little medicine bottle, and it has what to watch for, that may—if these prescriptions are renewed on a monthly basis or something, that may have been the time when people got the new information what to watch for, and I think a good pharmacist would have called attention to that.

But I think the reality of the healthcare out there, was—I suspect, almost none of the folks in the other system would have gotten the kind of somebody picking up the phone. But most private clinics don't have electronic medical records; they would not have been able to find the patients that had been prescribed that.

I think there's a lot of issues there that are part of the gaps in our healthcare system. I'm not saying that shouldn't be the goal. It should be the goal, but it's not there now.

In the outpatient clinics that the VA contracts out, of the patients that are on a medicine which gets some kind of warning—not just this medicine—what kind of a system do we think we have now in those clinics for notifying patients of a change? Or, again, are you just dependent on the practitioner?

Secretary PEAKE. You are talking about our community-based outpatient clinic (CBOC) contracts?

Mr. SNYDER. Yes, sir.

Secretary PEAKE. They're on the Computerized Patient Record System (CPRS), so they get the same information as the VA practitioners.

Mr. SNYDER. But they don't have electronic medical records?

Secretary PEAKE. No, they do.

Mr. SNYDER. They all have electronic outpatient records, so they can hit a button with a drug and pull up a list of all of the names of people who are getting that medication, do you think?

Secretary PEAKE. Yes. And when the November warning came—early communication came through, my recollection is that at Washington VA they actually ran the list and ran around and shared them.

And it just comes right out of the——

Mr. SNYDER. Because that clearly is the standard for the healthcare system in America.

Well, I am out of time. The final note, I would say—as you usually do, Dr. Peake—you learn from these things. The most unfortunate thing is, we have somebody there who is not doing a good job of recording the data of the study, and it can call into question the whole study. And then it calls into the question what's going on in

other studies, because the independent asking a question to the patient and not just copying off what somebody else asked them is a way of corroborating the information.

As you know, I am not telling you anything you don't know. I think that's the biggest glitch I see here today.

Thank you, Mr. Chairman.

The CHAIRMAN. Thank you, Dr. Snyder. Thank you.

Mr. BUYER.

Mr. BUYER. Mr. Chairman, I want to thank Dr. Snyder.

You went right to the question that I wanted to ask here on the standards of care, not just within the VA, but across the country.

Many States up there and the community health clinics are promoting utilization of Chantix®. Some States are paying for using it as a smoke cessation aid or drug.

And, you know, you have States out there, I will pick on the Chairman here for a second—California's State Department of Health recommends the use of Chantix®. However, a list of Chantix®'s side effects on the Health Department Web site has not been updated for 2 years. It does not reflect the FDA's latest findings, nor does it list the serious psychological side effects associated with Chantix® use, such as suicidal contemplations.

So you are probably right. All across the country, this is a medication that is being used.

You have the FDA, and your advisory here to the doctors, I think is pretty strong. I mean, you are telling them, you know, you need to let your patients know this.

I thought it was interesting that you also let the health providers know, Dr. Snyder, in the clinical trial that patients that may have had a psychiatric illness were not included in the clinical trial. I think that's sort of an interesting sort of note that the FDA has put in here, and maybe it even is intriguing on whether we should do a second look or not. I don't know. I'll leave that in the experts' hands.

But in their own advisory, when we had our witness testify, you come right out and say, patients should tell their healthcare provider about any history of psychiatric illness prior to starting Chantix®.

Mr. Elliott, even though he was taking this generic form of Prozac that had side effects—for instance, suicidal ideation—said that he was okay, he didn't have any of that at all. So I guess he didn't feel the need to inform, because he didn't have that thought.

But I find it interesting that you say that Chantix® may cause worsening of current psychiatric illnesses, even if it is currently under control. That's pretty doggone important. That's the advisory, I think, that goes right, Mr. Secretary, to the heart of this matter. I look at this one, and I made these comments about I feel like I am at a risk management hearing at a local hospital about a particular doctor. But then it can be, is it systematic?

Now when we talk about the standards of care—so when Dr. Snyder pointed out, I think aptly so, that perhaps doctors around the country might get a patient on Chantix®, or they're really going that far, as even noting a counseling on a medical record, well, that may be different. We can't control the standards of communities of care out there.

What we can control is our own community standard of care, for instance, the VA healthcare system. Would you not concur?

Secretary PEAKE. I would, sir.

Mr. BUYER. So, even though you can say, correctly so, that doctors are not required to have an addendum of the informed consent, would you not concur that if you want to establish the highest quality of care, that is something that we should have done and now should do in the future?

Secretary PEAKE. Within the study, I agree, it is something we should have done, because we said we should do it. And I think it—and it concerns me that—because, to my knowledge, we have about 50 percent of them done, only. I want to get to the bottom of why that is.

We have about, as you point out, sir, 32-, 33,000 people on Chantix® across the VA. I think it is the—the standard of care is appropriate that their physicians have been notified through their personal responsibility to keep up with the medical issue, but also through the additional push of information to the VA so that they are aware of what they need to do to best take care of their patient.

I would tell you, sir, that because of the headlines and so forth, I did send out a letter to 32-, 33,000, everybody that we have a record of being on Chantix®, encouraging them, first of all, to, if they have any of these side effects to include suicidal tendencies, thoughts, so forth.

So I sent them a personal letter saying, go see your doctor. If you have any concerns from what you've read about Chantix®, go see your doctor. We will find some other way to help you. If you are having any other kind of acute problems, here is our suicide hotline, here is how to get care.

So I think, as you say, sir, the standard of care issue is such that we should step beyond that, and I think we should.

Mr. BUYER. The last thing, Mr. Chairman, with your indulgence—it really kind of bothers me.

Dr. Puglisi, you have a position whereby this Committee created that position, and we didn't want these types of things to happen again.

We have a Washington hospital, call it Washington VA, which did not receive an accreditation. One of the failures was in the area of informed consent. So I look at this and go, we created your position to help the VA—and, in particular, the Secretary—and we have a particular hospital that's participating in a study that can't even get an accreditation on the human research issues.

Does this bubble to your attention? Have you got some concerns here? I don't get it.

Dr. PUGLISI. I have several concerns. I have concerns on the level of this particular study, and I have concerns system-wide.

In terms of this particular study, I'm concerned that it appears that at least some veterans who were prescribed Chantix® had never received written information about Chantix®. I'm concerned that at some of the study sites there appeared to be an undue delay in getting information to study participants.

I'm concerned on a systemic level that we apparently don't have the required mechanisms to make sure that these things are done in a timely fashion. I'm concerned any time informed consent ap-

pears not to have been adequate, because that's one of the keystones of human subject protections.

So to answer your questions, I am very concerned.

The Secretary has asked my office to look at these—this study in great detail, as well as all of the studies involving PTSD patients. And we will make very specific recommendations about how the system needs to be changed to make sure this doesn't happen again, and we will make specific recommendations relative to accountability of individuals who appear not to have fulfilled their responsibilities.

Mr. BUYER. Thank you, Mr. Chairman.

The CHAIRMAN. Thank you for that last statement. I am glad we are finally concerned.

Let me just conclude this panel. Several things bother me, as they bother Dr. Puglisi here.

First, Secretary Peake, you have incredible faith in this bureaucracy. I mean, there are almost 250,000 people at the VA. I don't know how this advisory went out, e-mail or circular. How did it go out?

Secretary PEAKE. Electronic, sir.

The CHAIRMAN. I mean, I go into my e-mail all the time. These guys have stuff in their in-box. Their e-mails are loaded up and I don't know who reads what. If it says FDA advisory, maybe they think its another one of 50 or 100 advisories. I don't know.

Secretary PEAKE. There are 50 a month.

The CHAIRMAN. Afraid so. That's why we are sending out——

Secretary PEAKE. That's why we have this system that says, which of these are really important. You've got 12 of them; you pop them and send them out.

The CHAIRMAN. Yes, but you don't know; you have no proof. In fact, we have the opposite proof the system is not working: 50 percent of the consent forms, in your knowledge. By the way, you said you are going to get to the bottom of that.

I mean, if I was sitting there, Secretary Peake, we are dealing with a very limited number of people in this study, 900 and something. Fifty percent haven't signed it, I would call up the 450 and say, get yourself to the doctor; and we'll get to the bottom of it. We will have a report, and there will be months and months that go by, and who knows what will happen in the interval.

I don't understand how you are going to get to the bottom of this? We have no proof of counseling. You said yourself that someone might come in six months later for their next appointment. They could commit suicide by then. We don't have any results, apparently, after 5 years of study. Your faith in the bureaucracy is overwhelming to me.

Second, the fact that everybody said—every quote I have ever read in any of the papers on this subject from Dr. McFall, to yourself, to anybody, this study is going to continue. It's as if the train started and nobody wants to stop it—it's going to continue at all costs. No causal connections have been made.

You said—and I just can't believe, Secretary Peake, that you said it doesn't matter which medicine, in terms of this study, to a very fragile group of people who have PTSD, were given something that was said to be possible suicide inducing.

Two hundred forty-five people are on that. Stop it, is what I would advise you.

You are going to go through another year of this study. You are going to get to the bottom of this. You have 245 people—although now, because of all the publicity, it may be down to 40.

I don't understand that, Dr. McFall or Dr. Puglisi.

Do you have the confidence to continue this study knowing what we know now?

Do you have the confidence, Mr. Puglisi? You said you had concerns. Would you consider this at all costs?

Dr. PUGLISI. I wouldn't continue the study at all costs. My review is going to be done on July 18, which is about 10 days from now, and at that time I will give——

The CHAIRMAN. When did you start that?

Dr. PUGLISI. June 18.

The CHAIRMAN. Well, I mean, wouldn't you just say, stop giving Chantix® for a month? I don't understand it.

Dr. PUGLISI. There are risks——

The CHAIRMAN. You are going by procedures, you are going by risks.

These people have PTSD. You are giving them something you know can lead to further thoughts of suicide—stop it.

Dr. PUGLISI. I would say that every person who has taken Chantix® or is now taking Chantix® needs to be notified immediately to consult with their physician.

The CHAIRMAN. Well, thank you.

Mr. BUYER. You haven't. The VA has not done that. You sent a letter out to 32,000 people.

Secretary PEAKE. Sir, we have 40 people on Chantix® now. Every one of them has been notified.

The CHAIRMAN. How?

Secretary PEAKE. Do you want to discuss that?

Mr. MCFALL. Yes, sir.

The CHAIRMAN. I would personally call all 40 and tell them to get to their doctor.

Did you call them? Did Secretary Peake call them?

If I were you, I would call them, Dr. Peake.

Mr. MCFALL. Mr. Chairman, what we can tell you is, all individuals who were on Chantix® as of February 1, 2008, which is when the FDA alert came out, have either been notified through the study staff or their provider.

The CHAIRMAN. You don't know that. You have asked the study staff to consult with them. You don't know that they have been consulted, right?

Mr. MCFALL. Through chart review.

The CHAIRMAN. Have you asked for a return saying, yes, you have notified them?

Mr. MCFALL. Let me check it out and let you know what we have. Maybe that will help.

The number of individuals, of those 120, who have a consent addendum signed is 56, and that leaves 64 that do not have a consent addendum signed. That's because the study visits haven't come up yet.

However, of those 64, they were notified by the provider who takes care of them or by the study staff.

The CHAIRMAN. I mean, how were they notified?

Mr. MCFALL. Through chart review.

The CHAIRMAN. I don't understand what that means. Does somebody call them——

Mr. MCFALL. Phone.

The CHAIRMAN. Did somebody call them and say, come in and see your doctor right away?

Dr. KUPPERSMITH. Uh-huh.

Mr. MCFALL. Well, the provider may have spoken.

The CHAIRMAN. Shouldn't they all have been called and told, come in and see the doctor right away?

Mr. MCFALL. What we can say is that the 120 people who had been on Chantix®, all have been contacted about the FDA safety risks published in February.

The CHAIRMAN. How have they been contacted? You said, either through their provider——

Mr. MCFALL. Either through the provider or the study staff, sir.

The CHAIRMAN. Do you know that they contacted them?

Mr. MCFALL. Yes, that's what we know.

The CHAIRMAN. How do you know? Is it on the chart or what?

Mr. MCFALL. Well, we asked them to have this data extracted.

The CHAIRMAN. You asked them to do it. How do you know that they did it?

Mr. MCFALL. Well, how do we know? Well, either we got the consent addendum back, it's in the records, that's been signed by the patient. So that accounts for——

The CHAIRMAN. How many of those have been?

Mr. MCFALL. Pardon me?

The CHAIRMAN. How many are those?

Mr. MCFALL. The number of people who signed the consent addendum was 56. So we have that many individuals.

The CHAIRMAN. You said that was the original process, and there were 64 that didn't.

Mr. MCFALL. Sixty-four didn't.

The CHAIRMAN. So how many of the 64 have now signed it, because they have all been notified, according to you?

Mr. MCFALL. What I can tell you, of the remaining 64 who had not yet signed a consent addendum, information about the risk from the FDA alert has been conveyed to all, either directly by the provider verbally or through a medical record documentation. That's 42——

The CHAIRMAN. Medical record documentation, that means they write it in a record?

Mr. MCFALL. They would write down in a record if they spoke to the patient about——

The CHAIRMAN. You said three times the same thing. I keep asking you, how do you know they actually did it?

Secretary PEAKE. What we have, sir, is a consent addendum signed, 56.

Of the 64 that we do not have a consent addendum signed, of those 64, it is documented in the medical record that they have

been notified and discussed with their provider, or with somebody, some member of the staff.

The CHAIRMAN. I would like to see those 64. I bet that hasn't happened.

So those 64 still haven't signed the addendum?

Mr. MCFALL. They have not signed the consent——

The CHAIRMAN. Then why do you let them continue in the program? Wouldn't you ask that, Dr. Puglisi? I mean, why are they in the program?

Dr. PUGLISI. The standard that the medical professionals determined was appropriate was to have individuals sign the consent addendum at their next visit to the study clinic.

In some cases, they have not had a study visit. However, I am not going to sit here and tell you that every person who is in this study had the opportunity to have a discussion at their next study visit or to sign the consent addendum. That's one of the things I am trying to find out.

The CHAIRMAN. That's the problem here.

Mr. BUYER. Dr. Puglisi, were these judgments by each of the individual institutional review boards? Is that why everything is so different?

It's hard for him to answer a specific question to the Chairman.

If you have different directives coming out from different institutional review boards about what docs are supposed to do, isn't that part of what the problem is, Mr. Secretary? Isn't that part of the challenge here?

Secretary PEAKE. It's why we want to go to a central—it's why we want to go to a central IRB. But I want to go back, so we can have consistency across this, and accountability, as I mentioned before.

But from the 1 February—as I say, across the course of the study, there are 241 who have been on Chantix®. Since 1 February, since this alert came out, there have been 120. That's the 120 that Dr. McFall is talking about.

All of them have been—we have documentation that each of them have been notified about the side effects.

Mr. BUYER. The Chairman—if I may be responsive here to the Chairman, because he—his point, I think, is probably pretty accurate.

You have 10 institutional review boards out there that now set all different kinds of standards on when an individual should receive their notice.

The Chairman's position is "now."

Secretary PEAKE. That's right.

Mr. BUYER. You would concur with that, Mr. Secretary, right?

Secretary PEAKE. That's right.

Mr. BUYER. And that's why you want to do these independent institutional review boards so they can feel your power and authority with regard to communication and oversight of this particular office; is that correct?

Secretary PEAKE. That's correct.

Mr. BUYER. I yield back.

The CHAIRMAN. I know you have nothing better to do, but I would call those 60 personally, Secretary Peake.

Let me just finally say the bureaucratic process goes on, there are still studies. I would have thrown some doubt on the fact of your in-depth study. It's internally by the very people you are trying to study. I have more confidence, having heard Dr. Puglisi's statement, so I will leave you alone on that one for now.

But, a bureaucracy study in itself is not what gives confidence to the public that it's been done.

I mean, if you want an independent study, you give me the 120 charts and I will read them. I will tell you, because I don't believe it, that all 64 were personally notified in a way that makes sense. That's how I would get accountability, not by asking the same doctor who is responsible for the study to tell me.

Ask me to look at it. Ask the Inspector General. Ask any of the staff here. Then I might believe you.

Secretary PEAKE. I was pleased that the Inspector General took on the task of taking a look.

The CHAIRMAN. If you want, give me the 120 charts, and I will tell you whether you have done the job or not.

Again, we are dealing with our children here.

I don't comprehend how all of you are sitting there, with all of your statements about clinical channels and how the clinical system is appropriate and that you have faith in the next study and that no one taking Chantix® is going to die from suicide.

I just can't imagine that you have so much faith in all these processes and all this bureaucracy—and if somebody does die, I will be at the trial to talk about your criminal negligence here—because the facts are with us, Mr. Secretary. Prudence says—if we talked about a bar being high enough and all of that, prudence says for these individuals who have PTSD, they have enough problems. Don't exaggerate it. Don't aggravate it.

You said, there will be millions of other things to stop the smoking, but that's not something we give to them. We are giving them the Chantix®, and that's our responsibility.

I can't believe that you all have 100 percent confidence that we are not causing a suicide.

You have the last word, Mr. Secretary.

Secretary PEAKE. Sir, I appreciate the chance to come here and talk about this issue. We actually don't agree, I think, on the issue of this medicine. I think you can find similar kinds of concerns about, really, any of the other smoking cessation therapy.

What we do agree on, sir, is an absolute commitment to our veterans and trying to do the absolute right thing by them. We absolutely do agree on ensuring that the integrity of the research that we do in the VA meets and exceeds the highest standards in this Nation, and I am absolutely committed to making sure that that happens.

The CHAIRMAN. You don't believe that 11 suicide attempts, attempted homicide, nine suicidal thoughts, six suffering from hallucinations doesn't give you pause? This is from your own study.

I don't know if you have studied the whole 32,000 or not.

Secretary PEAKE. It's about 70,000 that have been on Chantix®.

The CHAIRMAN. You studied all 70,000 for those symptoms?

Secretary PEAKE. Sir, those are the—this was not a scientific drug—that's the observations that we have about it.

The CHAIRMAN. That's my point.

Secretary PEAKE. That's why we are working with the FDA.

The CHAIRMAN. I thought you were going to say, it was only 0.05 percent of people attempting suicide, so it's nothing to worry about.

But what you are saying does not constitute a scientific study, you have this anecdotal data and you don't have pause about giving this stuff to these people?

Secretary PEAKE. That is exactly why we are working with the FDA to try to understand what is the best route.

The CHAIRMAN. Yes, but don't give it to them while you are working with the FDA. Have some prudence here. That's what I would advise.

Okay. We are on the next panel.

Dr. Subbiah, thank you for joining us. We had a two-person panel, but Dr. Koocher from the School of Health Sciences at Simmons College in Boston had to get to another appointment.

[The prepared statement of Dr. Koocher appears on p. 117.]

Dr. Subbiah is from Pfizer—I just want to get your exact title here—Vice President for Medical Affairs at Pfizer.

We would be interested to hear your thoughts on the process for human research subjects and relationship between pharmaceutical companies and researchers. Since it is your drug, what would you advise in this situation?

Mr. BUYER. Mr. Chairman, may I have a question?

The CHAIRMAN. Please.

Mr. BUYER. I have no objection if you want to combine panels three and four.

The CHAIRMAN. Okay. If panel four would join us also from the Inspector General's Office?

Mr. BUYER. Thank you.

The CHAIRMAN. We will save some time. Thank you.

Dr. Subbiah, you can begin, and then we will call on the others.

STATEMENTS OF PONNI SUBBIAH, M.D., M.P.H., VICE PRESIDENT, MEDICAL AFFAIRS, PFIZER INC., NEW YORK, NY; AND JOHN D. DAIGH, JR., M.D., CPA, ASSISTANT INSPECTOR GENERAL FOR HEALTHCARE INSPECTIONS, OFFICE OF INSPECTOR GENERAL, U.S. DEPARTMENT OF VETERANS AFFAIRS; ACCOMPANIED BY ANDREA BUCK, M.D., JD, SENIOR PHYSICIAN, MEDICAL CONSULTATION AND REVIEW DIVISION, OFFICE OF HEALTHCARE INSPECTIONS, OFFICE OF INSPECTOR GENERAL, U.S. DEPARTMENT OF VETERANS AFFAIRS; AND RANDALL SNOW, ASSOCIATE DIRECTOR, WASHINGTON, DC, REGIONAL OFFICE, OFFICE OF HEALTHCARE INSPECTIONS, OFFICE OF INSPECTOR GENERAL, U.S. DEPARTMENT OF VETERANS AFFAIRS

STATEMENT OF PONNI SUBBIAH, M.D., M.P.H.

Dr. SUBBIAH. Good afternoon, Mr. Chairman, Mr. Buyer, Members of the Committee. My name is Ponni Subbiah. I am a medical doctor and Vice President of Medical Affairs at Pfizer. I am responsible for the medical and scientific activities for products in the urology/respiratory area, which includes Chantix®. On behalf of

Pfizer, again thank you for the opportunity to speak with you today.

I would like to briefly address the following areas: the epidemic of tobacco addiction, the role of Chantix® in helping patients stop smoking, clinical trials and drug safety monitoring, and the recent updates of the Chantix® label.

As already mentioned, the World Health Organization has described tobacco as a leading, preventable cause of death. Worldwide, approximately 1.3 billion people currently smoke cigarettes. In the U.S. alone, more than 400,000 deaths are related to smoking each year. In fact, cigarette smoking is a risk factor for six of the eight leading causes of death in the world. Healthcare costs from smoking-related diseases are $75.5 billion annually.

It is important to understand that for most people smoking is not a lifestyle choice or habit, but rather an addiction to nicotine. Nicotine is a highly addictive drug, as addictive as heroin or cocaine.

Smokers become physically and psychologically dependent on nicotine. Quitting smoking, with or without treatment, is associated with nicotine withdrawal symptoms, and this may include irritability, anger, depressed mood and weight gain.

Quitting smoking has also been associated with exacerbation of underlying psychiatric illnesses, so it is very important to assess the benefits and risks of smoking cessation treatments in the context of this setting.

In the U.S., currently 21 percent of the population, in general, smoke cigarettes. By comparison, the smoking rate in the VA is 33 percent. The smoking rate in the PTSD patients ranges from 45 to 60 percent.

So Chantix® is the first non-nicotine-based medicine approved by the FDA in nearly a decade. It has been demonstrated to be more efficacious than a placebo as well as Zyban, which is another smoking cessation treatment that's available in the market.

Chantix® is not intended to be a long-term drug. It is indicated for use over 12 weeks and then an additional 12 weeks if the patient successfully quits. Today, Chantix® has been prescribed in approximately 7.5 million patients worldwide, 5.6 million of those in the U.S.

Consideration of benefits and risks of a medicine is a critical component of the dialog that needs to occur between the patients and their doctors. Gathering data to continuously inform that benefit/risk assessment is accomplished through various means, including the conduct of clinical trials and epidemiological studies. There are also clinical trials of Pfizer medicines, such as the trial that is the subject of this hearing, that are conducted independently of Pfizer.

Once the medicine is available in the market, any researcher can obtain the medicine and conduct studies without of the involvement of Pfizer. These studies may be funded from other non-Pfizer sources, such as academic institutions or the National Institutes of Health.

The Pfizer drug safety surveillance system is designed to continuously gather and analyze reports received about patient experiences with our products. These adverse-event reports are routinely shared with the FDA, as well as other regulators around the world.

The primary mechanism of communicating changes in a medicine's benefit/risk profile is the product label. It is common for the label to be revised numerous times in a product's life cycle.

With regard to Chantix®, there have been adverse-event reports of certain neuropsychiatric symptoms, including depressed mood, agitation, changes in behavior, thoughts of suicide and suicidal behaviors in patients attempting to quit smoking with Chantix®.

Reports of an adverse event does not necessarily mean there's a causal association between the product and the event. In the case of Chantix®, a causal relationship between these reports and the use of Chantix® has not been established. However, in some reports related to Chantix®, a causal relationship could not be excluded.

In November 2007, Pfizer worked with the FDA to update the Chantix® label to reflect these reports. Additional label updates were made in January and May 2008, respectively, to put this information on the warning section of the label to heighten awareness and to provide further guidance to physicians and patients about these symptoms.

The current label advises that a patient should stop taking Chantix® and contact their healthcare provider immediately if these neuropsychiatric symptoms are observed. Pfizer communicated these label updates to physicians, study investigators and other healthcare professionals through various routes, including updates to the product label, written communications, Web site updates and communications directly from Pfizer employees.

Patients also have access to this information through their healthcare provider, as well as through the Chantix® Web site. Based on our review of available safety information, including the adverse-event reports received to date, we believe the Chantix® label accurately reflects the product's efficacy and safety profile.

There are few things that provide greater health benefits than quitting smoking. It has been reported that nearly 70 percent of smokers want to quit. However, fewer than 7 percent of those who try are able to quit on their own. So given the devastating health effects of smoking, it is essential to have treatment options available to help smokers break free of nicotine addiction and stop smoking.

Thank you, and I would be happy to answer any questions you may have.

[The prepared statement of Dr. Subbiah appears on p. 105.]

The CHAIRMAN. Thank you.

Also with us is Dr. John Daigh, the Assistant Inspector General for Healthcare Inspections of the Department of Veterans Affairs, accompanied by Dr. Andrea Buck, who is a Senior Physician in the Medical Consultation and Review Division of the Office of Healthcare Inspections; and Mr. Randall Snow, who is the Associate Director of the DC Regional Office of Healthcare Inspections.

Thank you, Dr. Daigh, for being here. Is that how you pronounce it, "day?"

Dr. DAIGH. Yes, that's right.

The CHAIRMAN. Why don't you spell it D-A-Y like everybody else?

Dr. DAIGH. Yes, sir.

If I may ask, sir, that my written testimony be entered into the record.

The CHAIRMAN. Of course. Thank you. So ordered.

STATEMENT OF JOHN D. DAIGH, JR., M.D., CPA

Dr. DAIGH. I would just like to make a couple of comments.

One, we limited our review of this study to what happened at the Washington, DC, VAMC primarily. So that was the focus of the report.

The first thing I would like to say is that we do not interpret at all that there are dramatic deviations from human subject protections in this study, in that you had to sign consent in order to be—to determine whether or not you were a reasonable candidate for the study. You had to sign a second consent in order to be part of the study.

The problem from our point of view is that the study began and, over time, knowledge changed about the therapies for Chantix®. So where we have difficulty is, when it became clear, with the February warning, that there was a significant risk, and the DC VAMC IRB made the judgment that the patient should be notified, but the execution of that plan failed. And so that's the difficulty we have with the execution of this study as it stands right now.

I would have to say that the pharmaceutical staff reacted aggressively in taking the names of individual patients to the clinical leaders in the hospital so that they were aware of the patients under their charge who were on this drug. So we found that that effort on the clinical side, again separating out the world of research, was effective.

In a prior review, my office looked at VA's response to an FDA alert regarding tissue that was contaminated and should be pulled from the shelves. We published that in the last 6 or 8 months, and we found that there they also had responded very well. We had no significant issues derived from that review.

I do, however, have, in the work that we have done, we do believe that there are problems in the research community; and I think characterizing them as execution of the standard protocols and of performing the job that they are supposed to perform is an issue sporadically in our work that we have seen.

And I think that among the things that one needs to consider, in adjusting current business, is sunlight; that is, there are individuals at facilities and ORO who are charged with auditing protocols, looking at the research community, and ensuring that their reports do, in fact, make it to people who will take action, based on the findings of those reviews.

And so the problems that we have had and seen sporadically, in addition to the DC/VA are, are the protocols done in a manner that lends—is a protocol review done in a manner that lends credence to the fact that the audit is successful in determining or demonstrating how the performance of that protocol is, and then ensuring that the protocol—that those audit results, when shown to the proper authorities, that they take the appropriate action on that.

That would be the end of the statement I would have, sir.

The CHAIRMAN. Thank you.

[The prepared statement of Dr. Daigh, appears on p. 108.]

The CHAIRMAN. When you said the execution failed, did that include the notification from the doctor to the patient of the risk? Did that include the lack of an addendum to the consent form, the fact that when he came in for emergency care, he didn't get it?

Did you look at those issues?

Dr. DAIGH. What we did was, we picked the arbitrary timeframe of prior to the news media making a big announcement about this, and looked at the medical record to see whether the doctor noted in the medical record that there had been a discussion with patients regarding notification of problems with Chantix® for the study patients.

So you find, in my view, a failure that the IRB in DC decided that patients on Chantix® should have the amended review signed. And that did not get accomplished quickly, as you have already discussed.

But you do find in some of those charts, again, prior to June 20, that there was a discussion between their provider and that patient about risk of Chantix®.

The CHAIRMAN. In the case we heard today?

Dr. DAIGH. No, sir, I am not going to comment on any one particular case.

So it is a complex issue in responding to your question, given the time of cutoff that you look at when notification occurred.

So we believe that the IRB's plan to notify patients, whom they had a special relationship for because they were in the study, was not executed correctly.

The CHAIRMAN. Thank you. I hope we get some accountability for that.

Dr. Subbiah, I probably agree with everything you said in your statement, how important it would be to have such a drug.

The only thing that I would ask you about, or to qualify—and that's the root of this problem here—is that we were giving this drug to PTSD sufferers; and that's the real problem. That's why I think all of the witnesses who were up before you should have had some pause.

We are not talking about the average smoker, we are talking about people suffering from combat stress injury. Doesn't that alter some of the things you would say about how important the drug is, or doesn't the risk get heightened with those kinds of patients?

You made a general statement, that there are seven million—although we don't know how many of those have PTSD, but wouldn't that be a high risk?

Dr. SUBBIAH. Well, first, I think it is really important to step back and understand that patients with mental illness also have other illnesses that they can die from. So we know that patients who smoke—and specifically it has been shown that PTSD patients, not only 45, 60 percent of them, smoke, but actually many of them are heavy smokers.

And so, yes, they do have PTSD, but they can just as well have other comorbidities and actually die from sudden cardiac events and lung cancers and other illnesses.

So it is important that we continue to improve the standard of care, and options that are available to treat their other comorbidities, and so that is why I think research, in general,

should be continued not only in the general population, but also in subpopulations.

The CHAIRMAN. So you don't have any problem now of advising anybody who has PTSD and who is a heavy smoker to take it? You have no problem with that?

Dr. SUBBIAH. Well, I think, as indicated and as indicated on our label and with the changes, that any time that a patient who wants to quit goes to see his doctor, there has to be a communication and a discussion of the benefits and risks.

It's not just for Chantix®. It's with any prescription product.

The CHAIRMAN. I agree, but, apparently that didn't occur in all cases.

Has Pfizer done a study particularly with mental illness and Chantix®, or not?

Dr. SUBBIAH. We have a study currently ongoing in patients with schizophrenia, who—you know, that population, over 80 percent of them smoke. So that's currently ongoing.

The CHAIRMAN. Have you found anything worrisome about that one?

Dr. SUBBIAH. Well, as the research is ongoing, it's difficult to make conclusions on the results. So we are going to have to wait to get the results.

The CHAIRMAN. Does Pfizer have any consultant relationships with VA doctors?

Dr. SUBBIAH. So, as—you know, in general, Pfizer as a pharmaceutical company does have interactions with the VA. For example, so with all of our customers, if they want to use any of our products, we often interact with them to communicate the benefits, risks and efficacy and safety data of our products.

So, for example, we could have people such as our sales representatives, as well as people that interact with formularies, that could have have interactions with the VA.

The CHAIRMAN. That is not what I asked.

Do you have any paid consultants who work for the VA who are paid by Pfizer to consult on the use of drugs?

Dr. SUBBIAH. We do have—I am not aware specifically of paid consultants for the VA. But let me just comment generally on how we work with external experts and physicians.

The CHAIRMAN. I know how you work. That's what I am afraid of.

Dr. SUBBIAH. Can I answer the question?

The CHAIRMAN. Well, I would like you to get back to me. Do you have any paid people who work for the VA? You said you don't know. Can you get back to me with that answer?

Dr. SUBBIAH. Yes. So we can get an answer back to you.

The CHAIRMAN. How many and who?

Dr. SUBBIAH. Sure.

The CHAIRMAN. And, how much they are paid?

[The response is included in the answer to Question 5 of the Post-Hearing Questions and Responses for the Record, which appears on p. 134.]

Mr. Buyer.

Mr. BUYER. When did Pfizer become aware of the independently run smoking cessation research project being done by the Department of Veterans Affairs?

Dr. SUBBIAH. Are you referring to this particular study under discussion?

Mr. BUYER. Yes.

Dr. SUBBIAH. As far as I am aware, I personally became aware of this when we heard about the hearing from the—in *The Washington Times* article.

Mr. BUYER. You said "I personally."

Dr. SUBBIAH. Yes.

Mr. BUYER. You are here speaking on behalf of Pfizer, so I now know your personal opinion.

Were you aware of whether the VA ever gave any notification to Pfizer?

Dr. SUBBIAH. So there are two things. One is awareness and one is involvement.

Mr. BUYER. No. There is one specific question I have asked.

Dr. SUBBIAH. Okay. With regards to——

Mr. BUYER. Notification.

Dr. SUBBIAH. With regards to awareness of the study.

Mr. BUYER. No, Doc.

Dr. SUBBIAH. I am sorry. I don't understand.

Mr. BUYER. Notification.

Dr. SUBBIAH. Notification?

Mr. BUYER. Did the VA, anyone at the VA, ever tell Pfizer, we have an ongoing study on smoking cessation, and we are using your product? Do you know whether that notification, officially, ever happened?

Dr. SUBBIAH. I am not aware of any official communication. However, it is important to understand that there are Pfizer employees that do interact with staff at different VA centers, so there could have been some communication on the study. But there was no official communication, and there was no involvement by Pfizer in either the design, the conduct or the implementation of the study.

Mr. BUYER. Okay.

Now, let me ask the question of, had you known—okay, had you known, as a manufacturer of a product, that now that you are working in concert with the FDA to make sure that advisory opinions go out to medical providers, had you known that the VA was conducting this type of a study with individuals that have PTSD or other forms of neuropsychiatric disorders, what would your counsel have been to the VA?

Dr. SUBBIAH. Well, I can't comment on that particular study.

Mr. BUYER. All right.

Wait, wait, wait, Doc.

Dr. SUBBIAH. Okay.

Mr. BUYER. I will rephrase the question.

Now you know there's a study——

Dr. SUBBIAH. Yes.

Mr. BUYER [continuing]. Out there. What is your counsel to the VA with regard to the use of your product?

Dr. SUBBIAH. In PTSD or in general?

Mr. BUYER. With the use of your product in this VA research study, what is your counsel to VA?

Dr. SUBBIAH. That the benefits and risks of Chantix® should be discussed with individuals where Chantix® is being considered, whether it's in the clinical setting between the patient and the doctor, or if it's in the research setting.

The patient should be fully informed.

Mr. BUYER. Now that we know, though, that in your clinical trial—did not include individuals who have psychiatric illnesses or disorders, does that raise any concerns to you? Is this something that you as a manufacturer should take a relook, or the FDA should—in other words, if you don't do it voluntarily, obviously, it always could be directed.

Dr. SUBBIAH. So I think it's important to understand, then, the research during the development process. Because when we have a new molecule that we want to bring to the market, a specific disease area, we want to study it in a core group with people that have less comorbidities and less concomitant medications.

Because we need to figure out what—if there's benefits or risks, we need to figure out, is it from the drugs or is it from other things. So we try to minimize comorbidities.

Mr. BUYER. All right. I got you. I got you.

Dr. SUBBIAH. All right.

Mr. BUYER. Maybe it's me. Maybe we are two different pistons; you go up, I go down. We're not communicating very well here.

We now know that Chantix® as a cessation drug is being utilized in a study, right, that also incorporates PTSD. Now, let me just hold that because, Dr. Daigh, you had mentioned, quote, subjects could not be enrolled if they had a psychiatric disorder not in remission, were at imminent risk for suicide or violence or had severe psychiatric symptoms. So we wanted to make sure that—we are going to have a study, but we don't want to have any individuals that may have any of these particular symptoms that is not in remission. That is correct, right?

Dr. DAIGH. Yes, sir.

Mr. BUYER. Now we end up in a study whereby in the middle of that study we bring in Chantix®. So the original informed consent that were all signed by everyone, now we bring in a new drug. Now FDA says that drug has a side effect. We have this question about community standard, should there be an addendum with regard to informed consent. I look at this one now and go, all right, when you establish the protocols for the study, one of those protocols—one of those very important things that you are looking at is we didn't want individuals that may have a psychotic disorder not in remission. But if, in fact, we have now introduced a drug that could have a side effect of suicide ideation, I look at that and go we have a problem, we have a problem with the results of our study. Would we not here, Dr. Daigh, Dr. Subbiah.

Dr. SUBBIAH. I think what you had mentioned was that the patients that were not stable were not to be included in the study. That is two different things. So often, in general, when you do studies in mental illness, often you don't include unstable patients. But we need to continue to see how to improve care in these patients so you do continue to do studies as we are currently doing

a study in schizophrenia. But we make sure they are stable clinically before they are enrolled in the trial.

Mr. BUYER. Right. Then in the middle of your trial they end up taking a drug that causes them to be unstable. Do you continue having them in the study or do you move them out of the study?

Dr. SUBBIAH. Well, I think, first of all, it has not been shown based on data that Chantix® definitively causes all these symptoms. That is what we are continuing to study right now. The smoking cessation process is a very complex process. Smokers themselves are at a higher risk of suicide. The withdrawal process, regardless of having any treatment, has similar symptoms like depressed mood, irritability, anger, frustration. And then you have drug treatment. So it is important to remember these complexities when trying to make interpretations. And that is why it is important to continue to do research to be able to delineate this.

Mr. BUYER. When you do your clinical trials—I know I am over my time. When you do your clinical trials, it is also important that you understand the interaction of your drug with other drugs, correct?

Dr. SUBBIAH. Yep.

Mr. BUYER. So we had some testimony today by an individual who was taking this generic version of a Prozac that has a side effect of suicide ideation. And now—do you know whether or not in the clinical trial, were there other drugs that you studied in the clinical trial that it could have exacerbated these ideations?

Dr. SUBBIAH. Yes. So when you do a clinical trial—and in the Chantix® clinical trials what we do is we do continuously monitor for drug interactions and adverse events. So, yes, that is something we look for and then try to identify. But we can't base it just on one case. We have to look for what is going on between the treated group versus the placebo group and make comparisons.

Mr. BUYER. The last thing. I apologize, Dr. Snyder. I will get to you real quick. I know that the Chairman had the Secretary comment on that they are looking at Chantix®, you are looking at yourself, the FDA is looking at you and—because we have got a drug here that we know is helping people with regard to trying to stop smoking, otherwise it is going to kill them. Right? Do you have an ongoing study right now with regard to examination of the side effect for suicide ideation?

Dr. SUBBIAH. Yes. So in the studies—like, for example, in the schizophrenia study, we do have measures to look at suicide—there is a scale called the Columbia suicide scale. We have a scale that is looking at depression as well as anxiety, these are some of the other symptoms that we want to monitor for.

Mr. BUYER. All right. Thank you.

The CHAIRMAN. Did you tell the VA that you have that study?

Dr. SUBBIAH. No, I didn't.

The CHAIRMAN. If I were you, Mr. Secretary, I would just wait until their study is complete. Prudence. When will you have your study complete?

Dr. SUBBIAH. This will be done—the schizophrenia study will be done in 2010.

The CHAIRMAN. You'll still be around, Dr. Peake. Just wait.

Dr. Snyder.

Mr. SNYDER. I'd like to pursue that a little bit, Mr. Chairman, because it can be very easy for Secretary Peake and his folks to decide not to put a drug on the formulary. I mean, that could be a decision to say we are not going to include this drug. And what it would mean is that veterans who might benefit from it safely won't have the benefit of it. We used to say—I don't know—maybe General Peake didn't ever say this. But we always said never be the first one to start prescribing a drug and never be the last one to start prescribing a drug because—let the first guys be the ones that discover the side effects, but don't be the last guy in town that actually discovered a new treatment.

Well, I think we want the VA to have mainstream care. And if the medical letter which was referred to earlier—Secretary Peake referred to it—I used to subscribe to it back when I was practicing medicine. It was very helpful. It cut right to the chase and it gave you the big warnings. And when it says this is the best drug out there right now, you pay attention to that. And that is the kind of information—you are probably going to change your prescribing patterns. You are probably going to—not everybody liked the nicotine patches.

The CHAIRMAN. But the PTSD patient, that is the key here.

Mr. SNYDER. I think this is my time, Mr. Chairman. I have listened to you. Here is the issue. Let's talk about PTSD. I think we do a disservice to anyone with PTSD if we somehow say you have lost all your mental faculties and judgment to sit down with your doctor and make a decision about what is the best treatment for you. My dad had PTSD. He was a World War II guy. He was one of Patton's folks. And he got involved in burial details of guys who got burned and killed in tanks. It was terrible. And to the day he died he did not watch anything on TV but variety shows and game shows, no cowboys and Indian, no war, no crime. He didn't want anything that smacked of violence. Now, he didn't know he had PTSD, he didn't talk about PTSD. He died of his smoking. He went in to have a surgery and couldn't get off the ventilator and he died. Now, I don't think he was suicidal. I think if he had any inclination at all of what smoke would have done to him, and we have a better understanding now, he would gladly have sat down with a practitioner and said do you mean if I take that little pill I can get rid of this habit that is trying to kill me. But I don't have any reason to think that—well, anyway, I made my point.

I think we do a disservice to PTSD folks by somehow saying that they are not capable of making a decision with their doctor. There clearly are PTSD folks that have big time problems, but that is, I think, part of our job here is we want to convince the American public that just because someone has PTSD, it is a step toward doing better. It is not some kind of diagnosis that you are impaired forever. That is not what we are about. That is not what the VA is about.

So the only point I was going to make is I hope that what comes out of this today—I think this has been a pretty healthy discussion. I mean, research in big systems is always difficult, as General Peake can't pull strings on the hundreds and thousands of people that are out there. But I'd hate a signal to be going out there that for folks that have anxiety or bipolar disease or depression or

PTSD, that somehow the studies aren't out there yet, keep smoking, wait a few years, keep smoking, put those two or three packs away or keep puffing. I think that would be a terrible, terrible disservice, and I think what our goal is, is to have our veterans population get the same quality of care, if not better—I think it is better in a lot of cases—as they would out in the private world.

Right now that means a drug that seems to be proving most effective. That doesn't mean there is problems with how this study was conducted. And I think Dr. Daigh is getting at that and all, but I think we need to be sure what our ultimate message is. Our ultimate message is healthy people; even if you have PTSD, you can still get off cigarettes. If you have PTSD, you may want to discuss—I would encourage you to discuss in more detail what the side effects are of any medications just like you would if you had depression or anxiety or anything else. But it does not mean that you should wait a few years and be the last person in town to try getting off cigarettes. I think that would be a great disservice.

Thank you.

The CHAIRMAN. Thank you, Mr. Snyder. If I was unclear, no one is suggesting that such people are not capable of making those decisions. The issue is informed consent. And when you are offering that drug in a study and, one, you haven't given informed consent or signed anything, you are making it available at a time when you know there are problems. The doctor hasn't had the informed consent yet because we don't know what is going on with this thing.

Mr. SNYDER. I am just responding to your comment, Mr. Chairman, that you said prudence, Mr. Secretary, don't give the drug to anyone——

The CHAIRMAN. No. What I meant was that I wouldn't give the drug in this controlled study to those with PTSD. Don't give that drug in this controlled study.

Mr. SNYDER. Let me make sure I understand. So if a person with PTSD, a veteran, is going to a CBOC or going to their primary care doctor—and all people with PTSD, as you know, in the VA system don't go to PTSD clinics. They get their care through primary care. You are okay with them getting this medication as long as they are not in this study?

The CHAIRMAN. I am okay if they have completely discussed this with the doctor.

Mr. SNYDER. Oh, that's different than what——

The CHAIRMAN. That they are informed. We are talking about the study.

Mr. SNYDER. Then I misunderstood you. I thought all you said is prudence, pull the drug, don't give it to anyone with PTSD.

The CHAIRMAN. That's not what I said. I said pull it from this study. I am glad you clarified that because I agree with you. By the way, when you said you were appalled by the suggestion that we should stop research, I join you in that. That is not a message we want to give. The message I want to give is that in this controlled study where you have questions—as Mr. Buyer said—these people were supposed to be excluded and the warning from FDA said this could cause a recurrence of a past psychotic problem. So you are giving someone a drug that might—as he said, make the study invalid to begin with. That person should never have been

in it if that is what could occur. You subjected them to the condition to which you were trying to exclude, and I think there was a change in the middle of the study that created new problems that the veteran was not informed about. That is when I would have stopped it because a change had occurred and we should have used prudence until we knew more. I am not saying this to all 32,000 that we are giving this drug to—it was in this particular context.

But I thank you for your clarification. Last statement, Mr. Buyer?

Mr. BUYER. I have one in particular. Our colleague, Ginny Brown-Waite, wanted to be here. She is the Ranking Member on the Oversight and Investigations Subcommittee of the VA Committee. Her husband has Stage 4 cancer and obviously there is a medical emergency at the moment. So she is not with us here today.

Final two questions that I would have, Mr. Chairman, to Dr. Daigh. Do you have an opinion right now on whether these patients included in the study should continue to take Chantix®?

Dr. DAIGH. No. I answer it because——

Mr. BUYER. No, you do not have an opinion?

Dr. DAIGH. No, I do not have an opinion.

Mr. BUYER. Thank you. Is this—I am going to take the next step. Because I made comments earlier in the hearing about the importance of the doctor/patient relationship; it is the doctor that has the best interest of the patient at heart and is supposed to know and understand their human physiology and—which also includes mental. And they also want to be able to save their life through the smoking cessation, treat the mental disorder, and I don't want to interfere with that. We have an FDA approved drug that has specific side effects.

In your study that is going on, Dr. Subbiah, either now or maybe in previous studies, do we know the impact of alcohol on Chantix®?

Dr. SUBBIAH. So in the development program, patients were allowed to consume alcohol; however, patients who had history or diagnosis of alcohol dependence and abuse were excluded from the trials. In the registration trials, average patients reported consuming about one drink a day. So specifically that was what the patients had—we were studying it with regards to—as a concomitant medication. So we don't have any specific data on alcohol abuse but as, like Mr. Elliott, the normal use of alcohol was allowed.

Mr. BUYER. All right. So sometimes the doc gives you a drug, you say all right, don't take alcohol. That is not with Chantix®? You can take Chantix® and it is permissible to take alcohol?

Dr. SUBBIAH. Yes. Our current label does not indicate a contraindication in the use of alcohol.

Mr. BUYER. All right. Thank you. I yield back.

The CHAIRMAN. Thank you again. In the fifth century B.C., Hippocrates said—I am sorry. Mr. Scalise, I apologize. Do you have any questions?

Mr. SCALISE. No.

The CHAIRMAN. Okay. I am sorry. In the fifth century B.C., Hippocrates said, "first, do no harm." And I think that should be your

credo here, Secretary Peake. We don't know if we are going to do harm. I think the prudent thing is not to do harm.

I thank you all for being here. Secretary Peake, I thank you for staying for the entire hearing and listening carefully to what everybody has said. We hope that we can continue to do research and do no harm.

This hearing is adjourned.

[Whereupon, at 2:20 p.m., the Committee was adjourned.]

A P P E N D I X

Prepared Statement of Hon. Bob Filner, Chairman, Full Committee on Veterans' Affairs

I would like to thank the Members of the Committee, our witnesses, and all those in the audience for being here today.

I was appalled when *The Washington Times* published an article revealing that the VA was and continues to use Chantix® in Cooperative Studies Program #519—"Smoking Cessation Treatment for Veterans with PTSD." Some Veterans with Post-Traumatic Stress Disorder (PTSD) enrolled in a VA smoking cessation study were being, and continue to be, administered Chantix®.

Chantix® received FDA approval on May 11, 2006. However, on November 20, 2007, the FDA issued an early communication about an ongoing safety review of Chantix®. It revealed that FDA had received reports of *"suicidal thoughts and aggressive and erratic behavior in patients who have taken Chantix®."* At this point, the VA should have suspended the study and immediately notified all patients of the possible dangers.

The loss of a single veteran to suicide is a tragedy. Since December 2007, this Committee has held two hearings regarding the issue of veterans' suicide. This is why I fail to understand why the VA did not react when the FDA issued the early communication concerning the dangerous side effects of Chantix®.

On February 1, 2008, the FDA issued a Public Health Advisory stating: *"Chantix® may cause worsening of current psychiatric illness even if it is currently under control and may cause an old psychiatric illness to occur . . . symptoms may include anxiety, nervousness, tension, depressed mood, unusual behaviors and thinking about or attempted suicide."*

The VA waited until February 29, 2008, to send a letter and new consent form to study participants to notify them of the dangers associated with Chantix®. The letter informed patients that they may experience *"an increase in psychiatric symptoms such as anxiety, nervousness, tension, depression as well as untoward changes in behavior."*

But it failed to mention the fact that Chantix® may lead to suicidal ideation or attempted suicide. This fact was buried in the consent form.

Regardless, the warning was too late for Mr. Elliott, an Army veteran of OIF. In February, he suffered a psychotic episode that led to a confrontation with the police. Mr. Elliott, I appreciate your appearance before the Committee today and look forward to your testimony.

This is merely the latest incident in a series of events, from the suicides in Dallas to the e-mail suggesting VA providers downgrade the diagnosis of PTSD to "adjustment disorders" to the e-mail downplaying the epidemic of suicides in the VA, that have caused me and the other Members of this Committee to question the VA's accountability measures and also the Department's dedication to addressing the mental health needs of our returning servicemembers.

Today we will look at VA's procedures for handling human research subjects, determine whether they were followed in the design and execution of the smoking cessation study and explore whether there was adequate oversight of the study. Furthermore, I want to investigate VA's responsibility to respond to FDA advisories and VA's decision to continue to use Chantix®, a suicide-inducing drug, on veterans with PTSD.

But in a much larger sense, we use this hearing today to ask the VA when are you going to take responsibility, when will you hold people responsible for the numerous issues that have been identified over the last few months.

We see this in an email sent from Temple, Texas, stating that "given that we are having more and more compensation seeking veterans, I'd like to suggest that you refrain from giving a diagnosis of PTSD straight out. Consider a diagnosis of Adjustment Disorder."

We see this in Dallas, where, after four patients committed suicide this year, the psychiatric ward was forced to close. We see this time and time again, where we

hear soothing words like "responsibility" and "accountability," but we do not see action. Talk is indeed cheap, especially when it comes to the safety and well-being of our veterans.

It seems to me, and to other Members of this Committee, that the VA continues to follow the same old pattern . . . deny, deny, deny. And then when caught and confronted . . . cover up, cover up, cover up . . . or tend to try and minimize the importance of the issue, or show the veteran as an anomaly. But no one is held accountable and the system goes on.

When questioned, the VA immediately wants to defend "the process." When is the VA going to understand that it is not about the process, but about the veteran? When will the VA stop being the veteran's adversary and start being the veteran's advocate?

We are talking about people . . . we are talking about our veterans. Don't defend your process . . . defend our veterans . . . our heroes.

Prepared Statement of Hon. Steve Buyer, Ranking Repubican Member, Full Committee on Veterans' Affairs

Mr. Chairman, Thank you for yielding. I appreciate you calling this hearing so quickly.

The title of this hearing, "Why Does VA Continue to Give a Suicide-Inducing Drug to Veterans with PTSD," is certainly an attention getter; however, Mr. Chairman, I think it misses the mark.

With the possible exception of the physicians on our Committee, doctors Boozman and Snyder, I doubt that anyone on this Committee, including myself, have the expertise to determine which drugs should be used by VA.

I'll defer to the experts on that matter, and Chantix® has been an FDA approved drug since May 2006 and is used by over 7 million people world-wide to help them stop smoking. What I think this Committee should investigate, is whether VA failed to protect veterans who volunteered to be research subjects.

The VA Office of the Inspector General briefed our Committee staff prior to this hearing, and we know what their preliminary findings were. I am very disappointed that longstanding problems with the VA research program have apparently not been corrected.

Those problems relate to strict human research subject protections that require fully informed consent of patients before they participate in any research studies. It appears VA may have failed to disclose important facts veterans need to make informed decisions before participating in the study.

If they were not provided full information about the possible risks of their involvement in the VA smoking cessation study, this is a major problem, one that is made worse because it is not the first time there has been an informed consent problem in VA research.

During the 108th Congress, while serving here as the Chairman of the Oversight and Investigations Subcommittee, I introduced H.R. 1585, to establish the Office of Research Oversight within the Department of Veterans Affairs.

The language of this bill became Public Law 108–170. These provisions of this law established within the Veterans Health Administration (VHA) an Office of Research Oversight to monitor, review and investigate matters of medical research compliance and assurance in the VA, including matters relating to the protection and safety of human subjects and VA employees participating in VA medical research programs.

What gave rise to the legislation was an OIG report entitled "Alleged Research Improprieties and Informed Consent Issues, Jerry L. Pettis Memorial Veterans Hospital, Loma Linda, California" issued on October 7, 1999, along with several hearings that followed on VA research and informed consent issues.

The purpose of the legislation was to avoid the occurrence of situations like the unfortunate one we are here to discuss today.

The Committee was briefed on potential research misconduct at the Albany VA in January 2003. We were informed that the VA Inspector General and VHA were conducting an inquiry into the matter.

The clinical trial drug company sponsor detected clinical results inconsistent clinical trial data being submitted by the VA's principal investigator and brought that to his attention. This notification to the principal investigator turned out to be a flawed process, as senior managers were not apprised of this situation till much later and launched an internal investigation.

We closely monitored the progress of this investigation, but were informed that further updates would be limited as this had become a Federal criminal investigation.

This situation and many more incidents revealing weak departmental oversight in the protections of veterans in human and animal subjects research led me to create and legislate an independent oversight board to insure greater protections to vulnerable veterans that have volunteered to serve their country and volunteered to be subjects in clinical research.

Mr. Chairman, in August 2003, VA initiated a cooperative studies program, *"Integrating Practice Guidelines for Smoking Cessation into Mental Health Care for Posttraumatic Stress Disorder (PTSD)."*

This research project was to compare effectiveness of integrating smoking cessation with mental health treatment versus keeping them as separate treatment programs. The protocol medications for this research project included the nicotine patch and nicotine gum.

In January 2007, VA modified the protocol by adding Chantix® after FDA's approval of the drug for public use.

As of today, VA has approximately 32,000 patients on Chantix®, and the Department of Defense has approximately 67,000 patients on Chantix®.

On June 17, 2008, an article appeared on the front page of *The Washington Times* detailing the use of the drug Chantix® in the VA study, and the subsequent effects that may have been caused by this drug in one veteran in particular. That same day, I wrote a letter to the VA as well as to the VA Inspector General's office requesting an investigation and an immediate briefing on the allegations detailed in the Washington Times' article.

On June 18, 2008, I, along with Committee staff, and a representative from Congresswoman Brown-Waite's office attended the briefing with the Principal Deputy Under Secretary for Health; the Chief of Research and Development; the Chief Officer of the Office of Research Oversight; and the Acting Deputy, Chief Research and Development Officer. At this briefing, we were provided a chronology of events leading up to the Washington Times' article.

Committee staff again met with the Chief of Research and Development and the Acting Deputy, Chief Research and Development Officer on June 19, 2008, and requested all documentation of all amended informed consent forms for all study subjects, as well as all Adverse Drug Reactions (ADRs) and Serious Adverse Events (SAEs) related to this study that have been reported to VA's Cooperative Studies Center in Albuquerque, New Mexico.

To date, neither the Committee staff nor I have seen the amended consent forms. I asked the Secretary to be prepared to explain the absence of these forms during the question/answer period following his testimony.

Because of the preliminary findings, on July 3, 2008, I further requested a nationwide investigation by the Office of the Inspector General on human research subject protections. I'll have much more to say about this when Dr. Daigh of the Inspector General's office testifies.

The FDA and Pfizer are going to be testifying to inform the Committee about Chantix®. They are the only witnesses here today who can be considered experts or authorities on drug safety and Chantix®.

I caution my colleagues that this Committee lacks the expertise as well as the jurisdiction over the FDA and drug safety, for a topic more appropriately addressed by the Committee on Energy and Commerce.

To attack a drug as being unsafe and to characterize it as suicide-inducing is at best premature. We should be very careful in making sensational public statements about the safety of an FDA regulated drug without full information about it, when it could be of enormous benefit in saving lives.

Let us not jump to conclusions that we are poorly qualified to make. We should hear the testimony of the witnesses and their answers to our questions, and then only after careful inquiry make informed judgments on what occurred and what corrective actions and followup may be called for.

Make no mistake, we are all about accountability and if veterans have not been well served, I for one will not hesitate to aggressively seek appropriate corrective measures, including actions against VA officials.

Mr. Chairman, as you are well aware, the safety of patients at the Department of Veterans Affairs is of primary importance to those of us here on this Committee.

Thank you again, Mr. Chairman, and I yield back my time.

Prepared Statement of Hon. Harry E. Mitchell

Thank you, Mr. Chairman.

I appreciate you holding this hearing today to discuss the Department of Veterans' Affairs protocols and procedures following patient claims of mental health effects while participating in the VA Cooperative Studies Program #519, "Smoking Cessation Treatment for Veterans with PTSD."

While the goal of CSP #519, smoking cessation, is critical to the overall health of our veterans, there are several aspects of concern. Among these concerns are that accurate informed consent was not obtained from all participants, and those already enrolled in CSP #519 were not informed of possible serious side effects as new information from the FDA became available.

It is important to provide all information necessary regarding participation in such studies, and not doing so is simply unacceptable. While studies and tests are necessary for improving care, our veterans should never be subjects unwittingly.

Under your leadership, this Committee has made caring for the mental health of our veterans a top priority. We have repeatedly witnessed the serious needs of veterans at risk for suicide, and we must remain vigilant to treat these veterans with the highest quality of care available.

Our Nation's veterans have served honorably to protect us and our country. The least we can do is fight for them when they come home.

I yield back the balance of my time.

Prepared Statement of Hon. John T. Salazar

Good morning, Mr. Chairman.

I have been following the Chantix® story over the last few weeks and share your concerns over this incident.

Recent reports of the damage and mental breakdown experienced by veterans as a result of Chantix® are very disturbing.

Like my colleagues on this Committee, I question why this happened and if this is happening in other studies.

More importantly, I am interested in hearing the steps the VA is taking to ensure that this incident is not repeated.

For a veteran in a rural district like mine, seeking help can mean traveling over dangerous terrain and mountain passes in unpredictable weather.

Should one of them experience a mental breakdown the damage can be even more severe than if it took place in a big city.

I know that the almost 70,000 veterans that I have in my district go to VA centers expecting a system that is looking out for their well-being.

Many of the Veterans in Colorado's Third District are low income and live in rural communities.

Most have to travel long distances to get to their nearest VA facility.

However, they go through a great deal of hardship because they know that they will be receiving the best care available in gratitude for their service to our Nation.

It is this confidence that leads many veterans to take part in studies to better their lives and the lives of their fellow veterans.

We cannot dishonor their desire to continue to serve their fellow servicemen and women by not informing them of all the risks involved.

Our veterans need to be confident that they are safe when they go to a VA hospital, take their medications or take part in a VA study.

Incidents like this one shake their confidence in the system that is in place to care for them.

Veterans have given enough for this Nation and we must ensure that they have healthcare that takes care of their needs safely and effectively.

Mr. Chairman, I thank you and the Members of this Committee for the opportunity to review this incident to ensure that this does not happen again.

Prepared Statement of Hon. Steve Scalise

Mr. Chairman, thank you and Ranking Member Buyer for holding this important hearing on the VA smoking cessation program for patients with Post-Traumatic Stress Disorder (PTSD) and the alleged failure of the VA to promptly notify program participants of FDA health advisories, as well as documentation that informed consent procedures were properly followed.

It is important that we examine the process of how veterans in this study were informed of the side effects of prescribed drugs and whether they gave proper consent. More importantly, while we will hear testimony about drug safety, consent procedures, and bureaucratic oversight, we must remember that today's hearing is about the patients—the veterans who bravely served our country and now rely on the VA for proper healthcare.

Many of our veterans are suffering from PTSD as a result of their service to our Nation, including thousands returning from the conflicts in Iraq and Afghanistan. We must honor their service by ensuring they receive proper treatment, and we must make certain they are not taken advantage of for the purpose of clinical study.

I find it alarming when I read claims that veterans were not given adequate and prompt notification of the FDA advisories, as required by human research subject protections on informed consent. Furthermore, I am disturbed by the lack of informed consent documents in cases involving the Cooperative Study Program No. 519.

Veterans should be allowed to have a face to face conversation with their doctor about the treatment they are receiving, along with potential side effects, and the drugs they are taking so they can make informed decisions about their care. Discussing possible side effects and obtaining proper consent are vital to the doctor-patient relationship and the cornerstone of the human subject research. If veterans in this study did not receive adequate information about their treatment and did not consent, this threatens the validity and integrity of all VA research.

Mr. Chairman, I hope that our witnesses will address the notification and consent procedures involved in this study. And I hope that we gain a greater understanding of the procedures required to conduct medical research studies and what steps will be taken to hold anyone accountable if they did not follow the procedures.

Prepared Statement of James G. Elliott, Silver Spring, MD
(Iraq War Veteran)

Disposable Heroes

The Use of Veterans and Military Personnel as Research Lab Rats by the U.S. Veterans Health Administration

I. Timeline
II. Diagram
III. Select bibliography
IV. Binder with supporting research documentation

I. TIMELINE:

November 11, 2001, James G. Elliott enlist date—U.S. Army

James Elliott's experience while under the care of Washington VA Psychiatric Staff

October 30, 2007

A prescription for Varenicline was issued for James G. Elliott by the Washington VA Psychiatric Department after he was talked into enrolling into a study entitled "PTSD and Smoking Cessation Study #519". His prescribing physician, Hallie Lightdale, informed James that he was a *"good candidate for the study"* because he *"gives her good feedback."*

November 5–6, 2007

James received the prescription and began taking as prescribed.

Nov 12–13 (approx.), 2007

James began experiencing dermatological side effects (i.e. hives, uncontrolled itching) on the first day he took the full dose. The dosage instructions were to take ½ tablet by mouth every morning for 3 days, then take ½ tablet twice a day for 4 days, then take 1 tablet twice a day. James was experiencing serious dermatological side effects by the time he achieved the full dosage regimen as prescribed. As a result, he quit taking the medicine briefly until an appointment with his primary care physician, Dr. M. Villaroman, who advised James to cease taking Varenicline.

Nov. 20, 2007, First FDA warning on Varenicline regarding serious neuropsychiatric symptoms experienced in patients taking Varenicline.

VA does not notify study participants. James receives no warning but continues to receive mailed appointment reminders from the Washington VA to come in personally in order to complete the monthly study questionnaire.

Mid-December 2007

James attends his regularly scheduled appointment with Dr. Hallie Lightdale, his prescribing psychiatrist for Varenicline. She advised him to resume Varenicline at a reduced dose and dismissed side effects as temporary. James resumes taking Varenicline.

Early January 2008

James attends couples counseling with his fiancée due to his erratic behavior. The appointment is at the Silver Spring Vet Center with Gil Becker. Counseling was not successful because James' behavior during the session was not conducive to therapeutic interaction. His erratic behavior and emotional crisis continues to spiral downward.

Mid-January 2008

James attempts, in person and in an extremely agitated state, to see his psychiatrist Dr. Hallie Lightdale. He speaks with the receptionist, Evelyn Littlejohn, who says she will relay the message. He tells Ms. Littlejohn that it is an extreme emergency and that he must see a doctor. Ms. Littlejohn takes notes and James leaves without emergency treatment.

February 1st 2008, second FDA safety advisory on Varenicline/Chantix® regarding serious neuropsychiatric symptoms experienced in patients taking Varenicline. VA does not notify study participants. James receives no warning, but continues to receive mailed appointment reminders from the Washington VA to come in personally in order to complete the monthly study questionnaire.

February 5, 2008

James' behavior has become so erratic that his fiancée feels that the car keys need to be secured. He will not comply with her requests for the car keys, so she calls Montgomery County Police Department for assistance. James is then involved in a near-death situation/standoff with the police. He is tased for his own safety and secured by the police. He is hallucinating and reverts to combat-oriented behavior out of survival instinct. He does not recognize his own fiancée. His concept of time is so skewed that he perceives a 20-minute standoff with police as happening in a matter of minutes. He does not remember the entire event to this day. A straight-A, PTSD success story, Mr. Elliott is days away from a gala event for which he has been chosen to meet Colin Powell as a representative of successful, recovering veterans returning from theatre. Now, he is on the ground, tased and lucky to be alive.

February 8, 2008

Gil Becker, Silver Spring Vet Center Counselor, takes James Elliott from Montgomery County Jail to Washington VA. In a meeting with Dr. Stacey Pollack, Dr. Hallie Lightdale, and Gil Becker, he is told by Dr. Lightdale that the Chantix®/Varenicline is the likely cause of the episode. She stated, *"There had been problems with other people, but I never thought it would happen to you. I am so sorry, Mr. Elliott (para.)".* This is the only time to date that the Washington VA psychiatric department has admitted that Varenicline caused Mr. Elliott's February 5th psychotic episode.

February 9, 2008

James' fiancée, after close review of his medical files, realizes that he has been participating in a dubious research study. She meets with VA doctors, including Dr. Stacey Pollack and Dr. Hallie Lightdale. They offer no explanation for James' psychotic break. They accuse Ms. Hilburn of being controlling and overbearing. James is still suffering from Varenicline withdrawal. He is also overdosed on extended-release morphine that he is usually allowed to take as needed at home. He is forced to take 150 mg of extended-release morphine per day while hospitalized at Washington VA.

During the meeting, Ms. Hilburn holds up the booklet for study #519 and states that this is the "most heinous s*** I have ever seen." She also states, "My lawyer will kill me for saying this, but if it keeps you from prescribing Chantix® to even one more veteran, it will be worth any trouble we go through." The doctors rise and state that the meeting is over. They refuse to talk with Ms. Hilburn and shuffle James down the hallway. James is confused and unaware of the situation.

February 15, 2008

While hospitalized, James is forced to daily take 150 mg extended-release morphine at full dosage, even after VA doctors and staff were informed that he was allowed after a pain management class to take morphine as needed. James usually takes 50 mg extended release morphine every two days for severe, demobilizing back pain related to an inoperable combat-related injury (fall from roof through third floor of mortar-damaged house while on night raid). By February 14, James has ceased passing stool and has begun to have problems urinating, signaling potential kidney failure. Ms. Hilburn is advised by outside medical counsel to have James signed out and examined by private medical facility. Washington VA doctors force James to sign out AMA. Upon examination at a private medical facility, James is found to have a possible bowel obstruction and enlarged spleen. James is forced, due to legal constraints, to stay in a hotel, with no contact verbally or physically from his fiancée, for over a month. He cannot return home. He is alone, scared, wounded and betrayed by the VA. The Washington VA psychiatric staff is, by this time, only concerned with appearances and covering any indication that they were at fault. James is highly unstable, alone, and suffering withdrawals from a myriad of substances administered by the Washington VA.

James is lucky to be alive. There are likely many veterans who are not, due to this type of abuse at the hands of VA researchers.

We submit to the U.S. House of Representatives Committee on Veterans' Affairs this documentation in the hope that it will receive the deep investigation that it warrants. The actions taken by U.S. House of Representatives Committee on Veterans Affairs in relation to this submitted evidence will be judged by the American public and the international community and will determine, it is hoped, a new standard by which we care for our veterans and military staff in the United States.

The Hippocratic Oath is not alive and well in the Washington VA Psychiatric Department. We hereby ask for a criminal investigation in any death, suicide, attempted suicide, violent act or act suffered at the hands of any veteran or military personnel, civilian dependents or spouses that were enrolled in research programs conducted by the Veterans Administration to ensure that these situations were not caused by the same lapses in ethical medical conduct that were experienced by Mr. James Elliott. James Elliott was asked twice in closed offices "what it would take to make him happy". Each time, he told those that were asking this question that he wanted the testing to stop. He said that he wanted them to quit killing his friends.

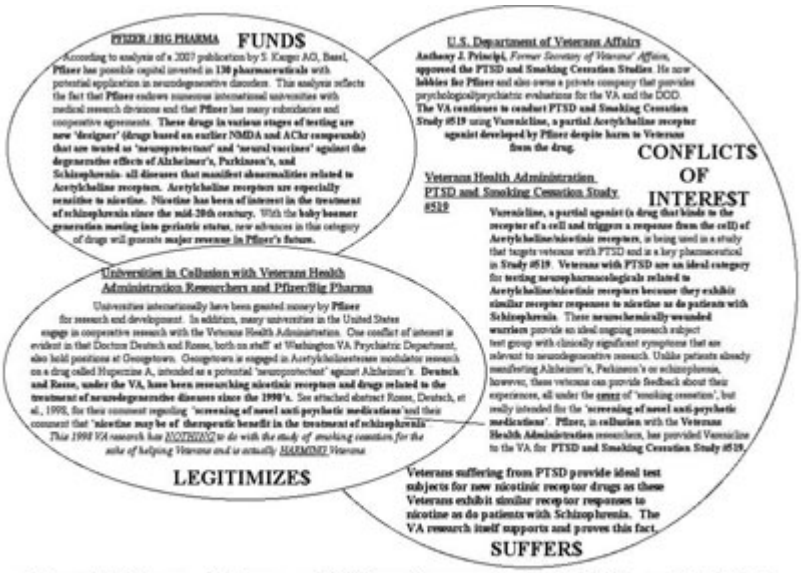
Please see the attached diagram for additional details regarding what Mr. Elliott and Ms. Hilburn learned after conducting research on Mr. Elliott's participation in the study, past VA studies and the ruse of smoking cessation as a benign and benevolent goal of VA medical staff. The information learned indicates unethical relationships between the U.S. Veterans Administration, Pfizer, its endowed universities and subsidiaries. The diagram details the research food chain in which Mr. Elliott found himself suspended without any recourse to due process.

Sadly, Mr. Elliott and other veterans were unwittingly used in this Nazi-like human medical research nightmare.

We maintain that the Veterans Health Administration should not be participating in medical testing on human subjects that have served our country. The Veterans Health Administration should be a place for veterans to heal, not heel.

James Elliott officially submits this evidence and information to the U.S. House of Representatives Committee on Veterans' Affairs for action as deemed necessary.

II. DIAGRAM:



Disposable Heroes : Veterans and Military Personnel as Medical Research Lab Rats

The Collusion of a Big U.S. Veterans Agency, Big Pharma, Big Research and Big Corrupt Bureaucrats

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Abstract Dizocilpine (MK–801) administration to an outbred strain of NIH Swiss mice elicits discrete episodes of explosive jumping behavior designated as "popping." ***This behavior may serve as a useful preclinical paradigm for the screening of potentially novel antipsychotic medications.*** Both nicotine and mecamylamine, a nicotinic antagonist, dose-dependently blocked dizocilpine-induced popping. The data suggest that nicotine may be of therapeutic benefit in the treatment of schizophrenia and that some of its effects may be mediated by non-nicotinic receptors.

Key words Dizocilpine—MK-801—Nicotine—Mecamylamine—Mice—Schizophrenia

Received: 17 December 1997/Final version: 10 March 1998

Select Bibliography

This bibliography is ordered in a timeline per category to show agency interest in psychosis and nicotinic receptors, historical perspective, and also corporate interest. Therefore, it is not formatted in the typical, academic fashion, but rather to show collective interest and connections. The research publications from a wider body of institutions and companies are submitted separately to the Committee in a binder prepared by Elliott and Hilburn.

Categories of research abstracts

I. Historical Interest in the treatment of Schizophrenia in conjunction with nicotine—1 abstract
II. Pfizer research on nicotinic receptors and Schizophrenia—1 abstract
III. Research publications focusing on nicotinic receptors and the treatment of Schizophrenia published through Mental Health Service Line, Department of Veterans Affairs Medical Center, Washington, D.C. and Linthicum, MD in

[1] Department of Pharmacology, College of Medicine, 520 W Street N.W., Howard University, Washington, DC 20059, U.S.A. Fax: +1–202–806–4453, U.S.

[2] Psychiatry Service, Department of Veterans Affairs Medical Center, 50 Irving Street N.W., Washington, DC 20422, U.S.A, U.S.

conjunction with Georgetown University and University of Maryland.—7 abstracts

IV. Research publications from the Department of Psychiatry, Veterans Affairs Medical Center, Denver, CO. with focus on the link between nicotinic receptors and Schizophrenia.—7 abstracts—not cited below but included in submitted binder.

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1. *Discovery of N-[(3R)-1-azabicyclo [2.2.2] oct-3-yl]furo[2,3-c] pyridine-5-carboxamide, an agonist of the alpha7 nicotinic acetylcholine receptor, for the potential treatment of cognitive defects in schizophrenia: synthesis and structure-activity relationship.* Wishka GD, Walker DP, et al. *J. Med Chem.* 2006 Jul 13; 49 (14): 4425–36.

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4. *Behavioral consequences of methyllycaconitine in mice: a mode of alpha7 nicotinic acetylcholine receptor deficiency.* Chilton, Mastropaolo, Rosse, Bellack, and Deutsch. *Life Sciences.* Vol. 74, issue 25, 7 May 2004, pp. 3133–3139.
5. *Therapeutic implications of a selective alpha7 nicotinic receptor abnormality in schizophrenia.* Deutsch, Rosse, Schwartz, Weizman, Chilton, Arnold and Mastropaolo. *Isr. J. Psychiatry Relat Sci.* 2005; 42 (1): 33–44.
6. *Effects of CDP-choline and the combination of CDP-choline and galantamine differ in an animal model of schizophrenia: development of a selective alpha7 nicotinic acetylcholine receptor agonist strategy.* Deutsch, Rosse, Schwartz, Schooler, Gaskins, Long and Mastropaolo. *Eur Neuropsychopharmacol.* 2008 Feb, 18 (2): 147–51. Epub 2007 Jul 26.
7. *First administration of cytidine diphosphocholine and galantamine in schizophrenia: a sustained alpha7 nicotinic agonist strategy.* Deutsch, Schwartz, Schooler, Rosse, Mastropaolo and Gaskins. *Clin Neuropharmacol.* 2008 Jan–Feb; 31 (1): 34–9.

IV. Research publications from the Department of Psychiatry, Veterans Affairs Medical Center, Denver, CO. with focus on the link between nicotinic receptors and Schizophrenia.—7 abstracts.

IV. BINDER:

Please see submitted binder for these abstracts and a selection of other related research abstracts. [The binder is being retained in the Committee files.]

Prepared by James G. Elliott and Tammy R. Hilburn

Prepared Statement of Lieutenant Colonel Roger G. Charles, USMC (Ret.), Vice-Chairman, Board of Trustees, Soldiers for the Truth Foundation, and Editor, *DefenseWatch*, on behalf of Eilhys England Hackworth, Chairperson, Board of Trustees, Soldiers for the Truth Foundation

Chairman Filner, and honorable members of the House Veterans' Affairs Committee, on behalf of Eilhys England Hackworth, Chairperson of the Board of trustees of Soldiers For The Truth Foundation, I am humbled to appear before your Com-

mittee as you carry out your responsibilities under the Constitution to exercise congressional oversight of the Department of Veterans' Affairs.

Recent events show that this oversight is critical to ensure that the well-being of our veterans is **in fact** the highest priority of the VA. These events demonstrate very clearly that without congressional oversight, true concern for the well-being of our veterans can deteriorate into mere lip service of an indifferent and self-serving bureaucracy.

I note that you have scheduled a most impressive group of experts on various medical and ethical issues related to human subject experiments as conducted by the VA.

I do not bring their expertise to this hearing.

What I do bring is the experience of a career Marine Corps officer who believes that our Nation has a sacred responsibility to care for those who have manned the ramparts of freedom on our behalf.

I also bring the skepticism of a journalist who for 18 years has investigated misconduct by various Federal agencies in the areas of defense and national security.

Let me now turn to the question that serves as the title for today's hearing. *"Why Does the VA Continue to Give a Suicide-Inducing Drug to Veterans with PTSD?"*

While studying the experience of Army combat veteran James Elliott, I was struck by three major questions which I believe this Committee's investigation should consider.

My first question relates to the Hippocratic Oath and a physician's first responsibility, "to do no harm."

How then did the VA physicians involved in planning and conducting this drug study fulfill their duties under this pledge?

Here are some "followup" questions I suggest you and your Committee staff might also consider:

- Would these physicians have subjected their own sons or daughters to such a high-risk drug study?
- And, would they have failed to inform their own children of the substantial risks this study entailed?

My second question relates to the Nuremberg Code, and the fact that informed consent of all human subject medical experiments is an absolute requirement under this code.

As you may recall, it was the exposure of the most heinous and gruesome medical experiments by Nazi doctors that led to enacting the Nuremberg Code.

Our country's own history has, unfortunately, too many examples of medical experiments on unwitting subjects. The infamous Tuskegee syphilis experiment is perhaps the best known of such shocking violations by physicians of their Hippocratic Oath.

I have attached to this statement a Knight Ridder press report dated July 7 that describes the latest legal action in a Federal criminal prosecution of a former VA staff physician at the Stratton VA Medical Center in Albany, New York. The Federal prosecutor asked the court to sentence this former VA physician, and I now quote from the press report, "to spend a year in prison for his role in a drug-research scandal that killed at least one veteran and victimized dozens more."

If it pleases the Chairman, I respectfully request that this article be included in the record.

My last question for your consideration involves the participants themselves, the veterans with PTSD, who were recruited by VA staff to become the subjects of this drug study.

Why were members of a group, who by the VA's own diagnoses were struggling to return to mental health normality, selected for this study?

The mental health of these veterans was known to have been, in various degrees, what a layman would term "fragile." Special caution and prudence should have been invoked before exposing them to a drug study where by definition "unknown" factors might further damage their mental health.

Instead, the very VA physicians trusted to help the vets regain a more normal mental condition enticed the vets to join a game of mental-health roulette, while withholding critical information that would have permitted true "informed consent" to have been given.

Sir, this concludes my prepared statement. I stand ready to respond to any questions the committee members may offer.

Doc in VA Drug Study Scam May Get Jail

July 07, 2008

Knight Ridder

ALBANY—Federal prosecutors want a former Stratton VA Medical Center oncologist to spend a year in prison for his role in a drug-research scandal that killed at least one veteran and victimized dozens more.

A year in jail is the maximum punishment that Dr. James A. Holland, 50, faces under his guilty plea last year to a misdemeanor charge in which he admitted failing to protect his patients from a rogue researcher who falsified medical records to enroll them in drug studies.

Holland's sentencing had been scheduled to take place in May, but was delayed as federal prosecutors and his attorney have made formal arguments about what punishment he should face. A new sentencing date has not been set.

"This crime was committed over a 3-year period, with many obviously altered documents involving a large number of cancer patients needing careful attention because of the gravity of their conditions," assistant U.S. Attorney Grant C. Jaquith wrote in a memorandum to U.S. District Senior Judge Frederick J. Scullin, Jr.

Jaquith argues in court papers that the high number of victims and significant financial losses to the drug companies and Department of Veterans Affairs warrants a maximum prison term.

Holland has placed blame for the scandal on Paul H. Kornak, 56, a former research coordinator at Stratton who posed as a doctor while advising patients and their families on life-or-death medical decisions. Kornak had a felony criminal record for lying on a medical license application when he was hired at Stratton. He never finished medical school and falsified his college transcripts to get there, records show.

Kornak was sentenced in November 2005 to a 6-year prison term for his guilty plea to felony counts of mail fraud and negligent homicide in connection with the death of James J. DiGeorgio, a 71-year-old Air Force veteran from Brunswick.

Another 64 veterans were harmed by the forgeries, which involved manipulating their medical backgrounds so they would qualify for drug studies that were lucrative for the hospital and had furthered the researchers' careers.

Federal authorities claim the research violations took place over about 3 years, beginning in May 1999. But VA workers have said the cancer program's problems, including the endangering of patients, stretched back years and involved other researchers.

Kornak blamed his actions on hospital officials, including Holland, claiming they urged him to enroll as many patients as possible in drug studies.

Gaspar M. Castillo, Holland's attorney, has cast Holland as a victim of Kornak and blames hospital administrators who allowed Kornak to masquerade as a physician.

"The defendant assumed, and it was reasonable for him to have assumed, that the VA had conducted appropriate background checks of Mr. Kornak," Castillo wrote last month in a letter to Scullin. Holland's guilty plea in April 2007 has not derailed his medical career. He works for a cancer program at Archbold Medical Center in Thomasville, Ga.

Holland and Kornak were fired by the hospital in 2002 after a private drug company investigator noticed problems with the medical records of patients. Authorities have never offered a clear motive for the forgeries.

A Times Union investigation found that Stratton's cancer research program was the target of internal complaints dating to the mid-1990s. Hospital staffers said they were harshly retaliated against for warning hospital administrators as early as 1994 that cancer patients were being placed at risk and being enrolled in drug studies without signing consent forms indicating they knew the risks.

Prepared Statement of Hon. James B. Peake, M.D., Secretary, U.S. Department of Veterans Affairs

Chairman Filner, Congressman Buyer, members of the House Committee on Veterans' Affairs, good morning. Thank you for the opportunity to appear here today to discuss VA Cooperative Study Program No. 519, our pharmacy benefits management program, and our work in protecting the health and well-being of veterans who volunteer to participate in our research studies. We share a common goal; to

provide the best healthcare available anywhere for our Nation's veterans; and all of VA's employees and volunteers work hard every day to ensure that this goal is met.

The Purpose of CSP–519

For more than 60 years, VA's research program has improved lives through innovation and discovery. VA researchers played key roles in developing the cardiac pacemaker, the CT scanner, radioimmunoassays, and improvements to artificial limbs. The first liver transplant in the world was performed by a VA clinician investigator. Clinical trials established the effectiveness of new treatments for tuberculosis, schizophrenia and high blood pressure. The Seattle Foot allows people with amputations to run and jump.

Recently, there have been questions and concerns with regard to VA research programs; in particular, with the VA Cooperative Study entitled "Integrating Clinical Practice Guidelines for Smoking Cessation into Mental Health Care for Veterans with Post-traumatic Stress Disorder (PTSD)" (CSP–519). This study is designed to determine whether integrating smoking cessation and PTSD therapies is more effective in stopping smoking than smoking cessation therapies delivered separately through a smoking cessation clinic, the usual way care is provided at VA.

Entering patients into the study began in November 2004, and ended in December 2007. The patients who entered the study all had PTSD, and all wanted to quit smoking. Patients in the study were allowed to receive medications from their healthcare providers to help them quit smoking. This is not a drug study. In many cases, the drugs patients are taking are prescribed by healthcare providers who are not at all associated with the study. Whether or not patients were enrolled in this study, all prescribing decisions were made by healthcare providers in one-on-one consultations with their patients, with those providers deciding which approach was most likely to work for those patients.

The study is being conducted at 10 medical centers, and 945 patients have been enrolled in the study. Patients participating in the study were randomly assigned into one of two study arms, and they were equally divided between those receiving integrated smoking cessation and PTSD therapies and those receiving smoking cessation therapies delivered separately through a smoking cessation clinic. All smoking cessation medications that were FDA-approved and on the VA formulary were made available to providers in both arms. Every patient enrolled in the study signed an informed consent form.

On June 20, 2008, VA's Chief Ethics in Health Care Officer provided me with her review of CSP–519. She concluded that the study aim is consistent with VA's mission to improve the health and well-being of veterans; the scientific design of the study was appropriate to address the research question and to yield useful data; the study does not expose patients to undue risk; the information about varenicline provided in the informed consent document was appropriate; the study's subject selection is appropriate; the study protocol adheres to ethical standards for privacy and confidentiality; the plan for monitoring the research is appropriate in terms of timeliness and thoroughness; the protocol reflects consideration and implementation of special safeguards to protect the rights and welfare of research subjects who may be vulnerable to coercion; and the remuneration offered for participation is modest, appropriate, and not coercive.

On June 25, 2008, I asked for a comprehensive review of the study—looking at whether protocols and safeguards were followed and met to ensure that our patients were receiving proper notice and quality care. I will discuss this in additional detail later in my remarks.

Importance of the Study

Every year in the United States, smoking accounts for approximately 440,000 deaths. Premature deaths from smoking rob more than 5 million years from the potential lifespan of those who have died. Forty years after the first Surgeon General Report outlined the health effects of smoking, smoking remains the leading cause of preventable death and disease in the United States. Smoking is a chronic, relapsing disorder, and even smokers who are highly motivated to quit may attempt to quit multiple times before they are finally successful.

Between 33 percent and 45 percent of smokers will die of smoking-related illnesses. The risk of dying from lung cancer is more than 23 times higher among men who smoke cigarettes. Smoking is associated with at least 14 other types of cancers, including cancer of the stomach, oral cavity, pharynx, larynx, esophagus, pancreas, and nasal cavity.

Cigarette smokers are 2–4 times more likely to develop coronary heart disease than nonsmokers. Smoking is also a major cause of cerebrovascular disease, chronic bronchitis, and emphysema, and is associated with gastric ulcers.

Smokers who quit before the age of 50 cut their risk of dying in the next 15 years in half. Smokers who quit have a slower rate of decline in lung function and a lower incidence of bronchitis, emphysema and other respiratory conditions than persons who continue to smoke. Quitting smoking reduces the risk for further congestive heart disease morbidity and mortality. Smokers with cancer who continue smoking during treatment decrease treatment effectiveness, overall survival prognosis and quality of life, and increase the risk for new morbidities. Smoking itself has psychiatric consequences. A recent study on smoking and suicide (Bronsich, et. al., Smoking predicts suicidality: Findings from a prospective community study, in the Journal of Affective Disorders 108 (2008)) found that suicide ideation and suicide attempts were strongly associated with occasional and regular smoking and nicotine dependence, with odds ratios from 1.4 suicides to 5.8 suicides among smokers to one among non-smokers.

Studies have shown that individuals with PTSD are more than twice as likely to smoke as the general population. While the rate of smoking among VA enrollees in general is approximately 30 percent, (Miller, D.R., et al., Health Behaviors of veterans in the VHA: Tobacco use: 1999 large health survey of VHA enrollees, VHA Office of Quality and Performance, 2001.) the rate of smoking among veterans with PTSD under VA care is 53 percent to 60 percent. (Beckham, JC et al, Prevalence and correlates of heavy smoking in Vietnam veterans with chronic posttraumatic stress disorder, Addictive Behaviors, September-October 1997.; Beckham, JC et al, Smoking in Vietnam combat veterans with post-traumatic stress disorder, Addictive Behaviors, September-October 1997.) Veterans with PTSD are more likely to be heavy smokers and are only half as likely to quit as are smokers without PTSD in the general population. VA believes it is our responsibility to help this population and all veterans to quit smoking, and we are continually working to find ways to do so.

The Use of Medications in CSP–519

CSP–519 is not a drug study. It is not a test of Chantix® or any other medication. The study was proposed, funded, and initiated before Chantix® ever came into existence. Instead, CSP–519 is a study comparing the effectiveness of two different methods for delivering standard, evidence-based treatments for tobacco use for veterans with PTSD. These treatments consist of behavioral counseling to stop smoking, which is required for study participation, plus recommended but optional medications for smoking cessation. Subjects could participate in the study without ever taking any medications for smoking cessation.

It is important to note that all medications have possible side effects. Attempting to regulate body chemistry by using medicines can have both beneficial and harmful effects. Two people who take the same medicine can have very different experiences. Physicians must always assess the risk of side effects against the expected benefits of any medication.

The side effects for any smoking cessation medication can be significant. Nicotine patches may cause headache, dizziness, lightheadedness, drowsiness, stomach upset, nausea or facial flushing. Patients wearing nicotine patches can experience more serious effects including breathing difficulties, chest pain, irregular heartbeat, nervousness, anxiety, tremors.

Buproprion, marketed as Wellbutrin® or Zyban®, can cause abdominal pain, constipation, decrease in appetite, dizziness, dry mouth, increased sweating, nausea or vomiting, trembling or shaking, trouble sleeping, weight loss, blurred vision, change in sense of taste, drowsiness, feeling of fast or irregular heartbeat, frequent need to urinate, unusual feeling of well-being, agitation, anxiety, tinnitus, skin rash, hives, itching, confusion, extreme distrust, hallucinations, seizure, and trouble concentrating. Overdoses can result in fast heartbeat, hallucinations, loss of consciousness, nausea, seizures, and vomiting. The FDA has required a "black box warning" for Buproprion stating that the medication, like all antidepressants, may increase the risk of suicide in persons younger than 25.

Varenicline, marketed as Chantix®, has been described by "The Medical Letter" publication as the most effective FDA approved smoking cessation medication available. During premarketing development of Chantix®, more than 4500 individuals were treated with the drug. Side effects of varenicline based on this clinical trial include nausea, which is fairly common; headache, difficulty sleeping, and abnormal dreams. Rarer side effects include a change in taste, vomiting, abdominal pain, flatulence, and constipation.

On November 20, 2007, the FDA issued an "Early Communication" based on postmarketing reports from users of the drug. In that message, they wrote that Pfizer, Inc., the manufacturers of Chantix®, had recently submitted to FDA postmarketing cases describing suicidal ideation and occasional suicidal behavior among Chantix® users. They also wrote that "Chantix®' role is not clear," and made several recommendations on more closely monitoring patients for behavior and mood changes.

On February 1, 2008, FDA issued a "Public Health Advisory" notifying healthcare providers that there may be an association between Chantix® and serious neuropsychiatric symptoms. It asked that patients and providers be made aware of this finding and stated that it appeared "increasingly likely" there may be an association between Chantix® and serious neuropsychiatric symptoms. To date, FDA has not asked that varenicline be removed from the market; has not issued a "black box warning" for the medication; and the drug continues to be FDA-approved.

Varenicline is one of approximately 62 FDA-approved drugs which, in their labeling, have been associated with or have concerns related to adverse effects that include suicidal ideation or suicidal behavior. These include a number of drugs with well-known brand names, including Neurontin®, Topamax®, Depakote®, Sustiva®, Cipro®, Accutane®, Lariam®, Reglan®, Provigil®, Abilify®, Clozaril®, Zyprexa® and Risperdon®. If VA were to withhold these medications from our patients with mental health issues, we would have great difficulties in treating them at all.

Approximately 6 million Americans have received prescriptions for varenicline. This figure includes 70,000 VA patients who have received prescriptions for varenicline since VA approved the drug in January 2007 for its formulary. Nearly 33,000 VA patients are currently taking the medication. Approximately 6,500 patients now taking varenicline have been diagnosed with PTSD. 2,012 of the 70,000 patients who have taken varenicline, including 400 of those with PTSD, are veterans of Operation Enduring Freedom or Operation Iraqi Freedom.

Two-hundred forty-one patients have been prescribed varenicline at some time during the course of the study, either by VA physicians or by physicians not associated with VA. As of June 25, 2008, VA is aware of 40 study subjects who are currently taking this medication.

A review of Serious Adverse Effect data among CSP–519 participants indicates that, from January 1, 2007 through June 25, 2008, of the 241 patients prescribed varenicline, 75 had a total of 114 significant adverse effects. Nineteen of those seventy-five had 22 psychiatric significant adverse effects, including 11 patients who had 12 episodes of suicidal ideation. There was one suicide attempt in that group, and no suicide completions.

Of the 704 patients who were not prescribed varenicline, between January 1, 2007 and June 25, 2008, 124 unique patients had 171 significant adverse effects during the study. Twenty-eight of those patients had 36 psychiatric significant adverse effects, including 11 patients who had 14 episodes of suicidal ideation. Four patients who were not prescribed varenicline attempted suicide, and one committed suicide. There was one intentional drug overdose, not yet classified as suicide. It is important to note that adverse effects occur during studies which are unrelated to the study itself. Throughout the entire course of the study, there were two deaths, unrelated to the study, in the group of patients taking varenicline. There were also 25 deaths in the group that did not take varenicline, which have not been analyzed.

The patients participating in this particular study, or any VA study, are under the care of physicians who are closely monitoring and evaluating them and changing their treatment if necessary. The care of our patients is our number one concern whether the veteran is participating in a study or not.

Patient Awareness of Issues Related to Varenicline Use

On the national level, VA quickly responded to FDA communications about varenicline. FDA's November "Early Communication" was distributed to all VA facilities the day after it was issued. Once VA received the preliminary message, we aggressively searched for events which might signal a problem among our patient population. This was done not only through an evaluation of the voluntary reporting of adverse drug events throughout our system, but also through the use of VHA's integrated medication databases to search for any potential safety issues.

On January 18, 2008, VA issued guidelines to providers stating that varenicline "should be reserved for veterans who have not been successful with nicotine replacement therapy and/or buproprion, or for whom buproprion is contraindicated." It also stated that before starting varenicline treatments, VA healthcare providers should educate veterans about the possibility of changes in behavior and mood, and they should be carefully monitored, and that veterans using varenicline should be warned that it can cause drowsiness and should use caution while driving or operating machinery.

On February 24, 2008, after testing at three medical centers, VA provided updates for local medical centers to their prescription software. The updates provided additional labeling on prescriptions for varenicline. It stated "Call your doctor immediately if you have mental/mood changes like confusion; new/worsening feelings of sadness/fear; thoughts of suicide, or unusual behavior." By April 1, all VA facilities except one had completed this update. VA also provides patient medication information sheets on all new and renewed prescriptions. Information on those sheets was updated in the same way.

Institutional Review Boards (IRBs) at all CSP–519 study sites were notified of the FDA "Public Health Advisory" on February 5. On February 13, the study coordinators sent all study leaders a new patient consent form for patients in the study to sign who were taking varenicline. They also sent a draft letter for patients informing them of the FDA's warning. The draft letter was written by a team of psychiatrists and psychologists who felt the issue of suicide should be discussed in a clinical setting, not a mass mailing, when patients reported to their study coordinators for regular follow ups. It did explicitly advise patients that they should inform their doctor or the study staff immediately if they noticed any changes in their mood or behavior, or if they would like to stop using the medication.

The cover letter was never intended to serve as a stand-alone document that would duplicate the consent addendum, which was attached. Instead, the purpose of the cover letter was to provide a brief and concise introduction to the addendum—an addendum that explicitly listed all the potential side effects identified by the FDA's warning, including suicidal ideation and suicidal behavior.

The timing of mailings of the letter and the consent form addendum were left to the individual IRBs. VA's agreement with study participants indicated that if any new specific information became available related to the study we would inform them, and study leaders felt that the FDA "Public Health Advisory" met that standard.

This plan was formulated by the CSP–519 study team, which included a physician; a pharmacist; a psychologist; a social worker; and other representatives of the CSP Pharmacy Coordinating Center, the CSP Coordinating Center, and the study Chair's office. The plan was approved by the CSP Human Rights Office and the CSP–519 Executive Committee, and was overseen by the CSP–519 Data Safety Monitoring Board.

Letters to patients were sent or hand-delivered between February and June. I am concerned about the time that elapsed at a number of study sites between the receipt of the letters and consent addendums by IRBs, and when they were received by veterans. I am also concerned about the lack of followup by study coordinators to ensure that their directions were carried out. There is a clear need for improved follow up in this area.

Since March 2007, the VA Center for Medication Safety has monitored varenicline through national pharmacovigilance efforts such as collecting and analyzing spontaneous reports of adverse events. As a result of their data, FDA's Public Health Advisory, and the Federal Aviation Administration's banning of the use of varenicline in airline pilots and air traffic controllers, VA issued a National Pharmacy Benefits Management Services Bulletin on May 30 to all practitioners informing them of the new warnings. They also sent a Patient Letter for Formulary Leaders and Pharmacy Chiefs to provide to their patients. Following news reports on the issues at this hearing, I sent a letter June 20 to all 33,000 patients with a current VA prescription for varenicline, offering to find another way to help them quit smoking if they were concerned about taking varenicline or had experienced any side effects.

VA has consistently and continually provided FDA with information on our experience with varenicline, and is continually looking for evidence to indicate whether its use should be continued in our patient population. To date, however, we have found no evidence that would cause us to discontinue the use of this drug in our patients. No other healthcare system approaches the vigilance VA has demonstrated in educating its providers and patients on the possible newly reported risks of varenicline. The care, treatment, and health of our patients is our number one concern. The research we do benefits them as well as patients throughout the world.

Safeguards and Protections in VA's Human Research Program

VA research, done with patient consent, benefits veterans; all Americans; and all citizens of the world. VA gratefully acknowledges the contributions of veterans who volunteer to participate in our research and we take our responsibilities for their care very seriously. In the past 7 years alone, VA employees have authored or coauthored more than 46,000 scientific articles. Nearly 900 were published in the most eminent of the Nation's scientific journals, including Science; the New England Journal of Medicine; and the Journal of the American Medical Association.

VA's Cooperative Study Program (CSP) specializes in designing, conducting, and managing multi-site clinical trials and epidemiological research. These include studies establishing the cornerstone for hypertension treatment; the long term effects of coronary artery bypass surgery; a study showing that aspirin reduces deaths and heart attacks in patients with unstable chest pain; and a study demonstrating the efficacy of a shingles vaccine. Just last week, the New England Journal of Medicine published the latest CSP contribution, which compared intensive versus standard therapy in patients with acute renal failure. The VA Cooperative Studies Pharmacy Coordinating Center is ISO 9000 compliant, and has received many awards for its effective management of clinical trials.

VA policies and procedures in this area are among the best in the Nation. Every VA research facility must have an IRB, the local Committee charged with the oversight of all research activities involving the use of human subjects. IRBs must have at least five members with varied backgrounds to promote complete and adequate review of research activities; at least one member whose primary expertise is scientific and one whose primary expertise is non-scientific; and at least one member not otherwise affiliated with the VA medical center. No IRB may consist entirely of members of one profession.

IRBs must approve, require modifications to, or disapprove all research activities. Before approval, they must determine that the following requirements are satisfied: risk must be minimized; there must be a reasonable risk to benefit ratio; subjects must be equitably selected; informed consent forms must be valid; the informed consent process for patients must be documented; safety must be monitored; privacy and confidentiality must be maintained; vulnerable subjects must be protected; conflicts of interest must be managed, reduced or eliminated; and investigators must meet education requirements for the protection of human subjects in research. All IRBs are required to fully document their activities.

VA's CSP goes above and beyond what other organizations do in the area of human subjects protection through our Human Rights Committees, which determine whether protections of patients' rights and welfare in VA research studies are adequate. These Committees are composed of individuals from the community and VHA with the interest and background required to consider the ethical and legal issues involved in the participants of human subjects in research. They are also responsible for ensuring that patients' rights and welfare are protected during studies, and for talking directly to patients to ensure that human rights aspects of cooperative studies are receiving proper attention.

VA has established numerous other safeguards for our patients in VA research studies. We are one of sixteen federal agencies who have adopted the Common Rule for the protection of human subjects in research. In 1999, we established an independent office of research compliance and assurance. This office was succeeded, in 2003, by the Office of Research Oversight (ORO), VA's primary office responsible for overseeing the responsible conduct of research throughout our system. In 2003, its first year of operations, ORO made 19 site visits to facilities. In 2004, that number increased to 22 visits; by 2007, it had tripled, to 67.

In 2001, VA published a brochure to help veterans understand their rights as research volunteers and to decide whether they want to be research participants. This was followed, in 2003, by the publication of a handbook describing the procedures all our research facilities must use to implement our agreement to follow the Federal Policy for the Protection of Human Subjects.

In addition, VA has developed a program to accredit all VA research programs by the Association for the Accreditation of Human Research Programs. In 2003, we required all VA employees involved in human research support programs (except secretaries) to undergo annual training in good clinical practice and the ethical principles of human research protection. More than 15,000 employees completed the training within 90 days of its establishment. Since 2003, we have created more than 15 different training programs in human research protection for our employees.

Also, we have established a Central Institutional Review Board to preclude some of the variability we have seen in execution of multi-site projects such as CSP–519.

Actions Underway

Though VA research is regularly reviewed by many organizations, we have directed that each VA human subject protection program must seek accreditation through the Association for the Accreditation of Human Research Protection Programs. At present, 112 of 115 VA facilities conducting human subject research have submitted applications for accreditation to this organization; all will be reviewed by the end of Calendar Year 2008. Of these 112 facilities, 57 have already received full accreditation. In some cases, this supplants previous accreditations received from

the National Committee for Quality Assurance (NCQA). VA leads all federal agencies in accreditation of human research protection programs.

VA's National Research Advisory Council, which is composed of internationally recognized medical scientists, has consistently recognized VA's research program for its success in meeting its obligations to taxpayers and to veterans.

While we have procedures and safeguards in place for the protection of our patients, I am committed to making sure we are doing everything we can on behalf of our Nation's veterans. On June 25 I directed the Under Secretary for Health to conduct four evaluations:

First, I requested a comprehensive review of CSP–519, through VA's Office of Research Oversight, with results to be reported to me within 30 days and with an action plan to address recommendations to be completed not more than 10 days later.

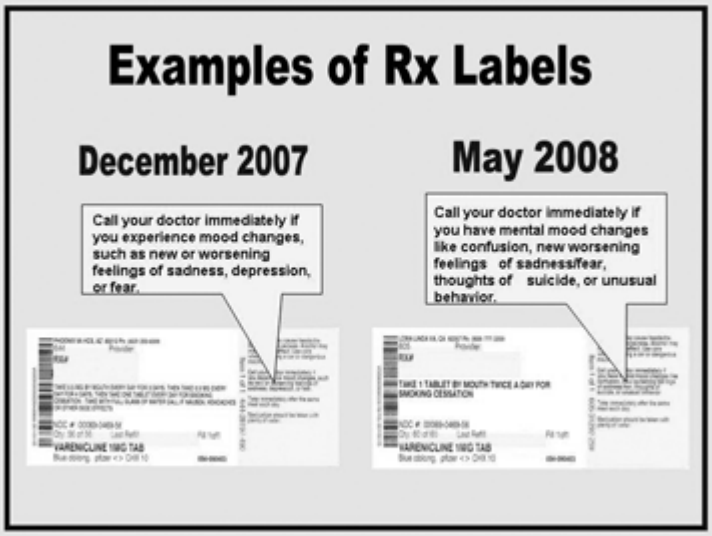
Second, despite the fact that CSP–519 is not a drug study, I directed that there be Institutional Review Board reviews of all PTSD drug protocols in our system to ensure that there is appropriate sensitivity to the study population in the context of FDA alerts and warning. I also directed a review of the risks of medications that are likely to be used in the study population, and that there has been proper subject notification of associated risks. The Office of Research Oversight is to report results to me within 45 days, and the Under Secretary for Health will provide me with an action plan 10 days later.

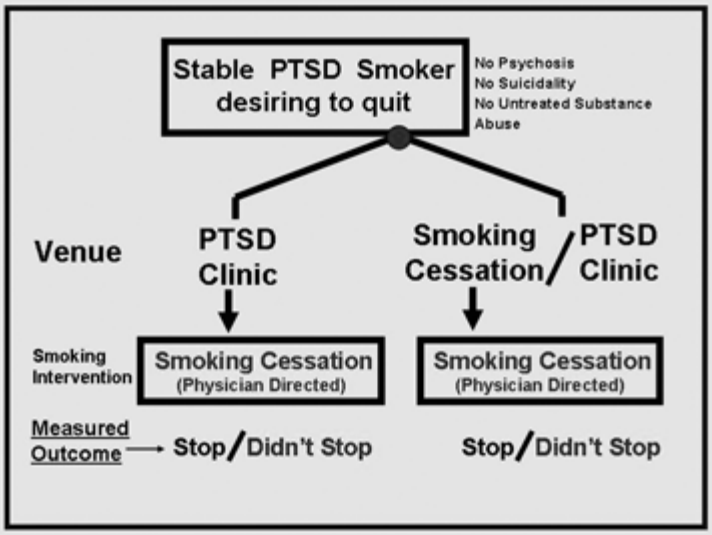
Third, I tasked the Office of Research and Development and the Office of Pharmacy Benefits Management to conduct a review of our adverse event reporting system to ensure that there is, in fact, timely reporting and analysis of data, and that the system supports the appropriate escalation of reporting and sensitive issues for subject safety. I expect their results within 20 days, with action plans provided 10 days later.

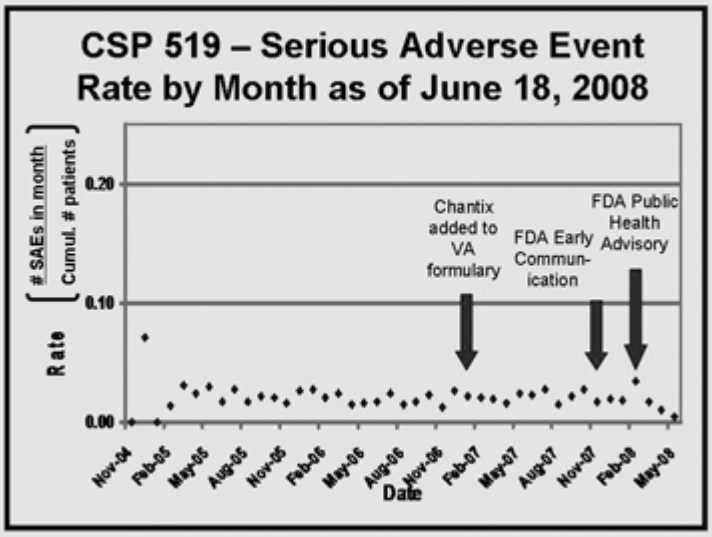
And fourth, I required the Office of Pharmacy Benefits Management to review VHA's medication notification system to ensure the system's policies support timely communications to patients and providers, including those in research programs. Results here are to be reported within 20 days and action plans provided 10 days later.

In addition, the Inspector General is investigating human subject protections in CSP–519 at the Washington VA Medical Center. He will testify on what he has learned later in this hearing. He and his staff have discussed his findings with me. I appreciate the speed with which he prepared his report, and have appreciated his consideration on clarification of some factual matters.

I have tremendous sympathy for any veteran who has been distressed by reports about this study. At the same time, VA has an outstanding research program, and has been innovative in its ability to protect its research subjects. I commit to veterans, and to you, that I will be comprehensive and thorough in my investigations of how this study has been, and is being, conducted. I am determined that VA will remain a leader in the protection of human subjects and in veteran-centric research. Thank you again for the opportunity to discuss the important work we were doing for and with the help of veterans.


Examples of Rx Labels
December 2007
May 2008
Call your doctor immediately if you experience mood changes, such as new or worsening feelings of sadness, depression, or fear.
Call your doctor immediately if you have mental mood changes like confusion, new worsening feelings of sadnessfear, thoughts of suicide, or unusual behavior.


Stable PTSD Smoker desiring to quit
No Psychosis
No Suicidality
No Untreated Substance Abuse
Venue
PTSD Clinic
Smoking Cessation / PTSD Clinic
Smoking Intervention
Smoking Cessation (Physician Directed)
Smoking Cessation (Physician Directed)
Measured Outcome
Stop / Didn't Stop
Stop / Didn't Stop


CSP 519 – Serious Adverse Event Rate by Month as of June 18, 2008
SAEs in month
Cumul. # patients
Rate
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Chantix added to VA formulary
FDA Early Commun-ication
FDA Public Health Advisory
Nov-04
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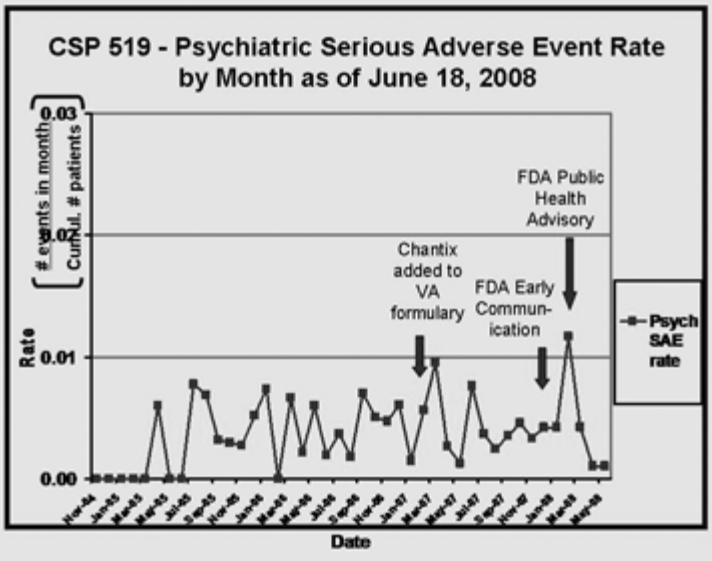
CSP 519 - Psychiatric Serious Adverse Event Rate by Month as of June 18, 2008
events in month
Cumul. # patients
Rate
0.03
0.02
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FDA Public Health Advisory
Chantix added to VA formulary
FDA Early Commun-ication
Psych SAE rate
Date

Department of Veterans Affairs

Memorandum

Date: June 23, 2008

From: Secretary (00)

Subj: Evaluation of Research

To: Under Secretary for Health (10)

1. In response to recent allegations I direct you to conduct evaluations of VHA Research and related support functions as outlined below:

a. *Part I:* The Office of Research Oversight (ORO) will continue a comprehensive review of Cooperative Studies Protocol #519 (Integrating Practice Guidelines for Smoking Cessation into Mental Health Care for Posttraumatic Stress Disorder [PTSD]) consistent with the plan outlined by the Chief Research Oversight Officer (see attachment). ORO should report results to me within 30 days. I expect an action plan to address ORO's recommendations within 10 days after the report has been completed;

b. *Part II:* ORO will oversee Institutional Review Board reviews of all PTSD protocols to ensure there is: appropriate sensitivity to the study population in the context of FDA alerts and warnings; a review of the risks of medications likely to be used in the study population; and proper subject notification of associated risks. ORO should report results to me within 100 days. I expect an action plan to address those recommendations within 10 days of the report's completion;

c. *Part III:* The Office of Research and Development (ORD) and the Pharmacy Benefits Management (PBM) Strategic Healthcare Group will conduct a review of the adverse event reporting system in investigational and clinical settings to ensure there is timely reporting and analysis of data and that the system supports the appropriate escalation of reporting and sensitivity issues for subject safety. The review should also address triggers for reporting or escalation of reporting. ORD should report results to me within 20 days. I expect action plans to address the recommendations within 10 days afterward; and

d. *Part IV:* The PBM will conduct a review of the Veterans Health Administration medication notification system to ensure that the system's policies support timely communication to patients and providers, including those in research programs. Recommendations from the review will be coordinated with Operations, ORO and ORD to ensure policy coordination. PBM should report results to me within 20 days. I expect an action plan and revised policy to be completed within 10 days of the report.

2. If you have any questions about these tasks, please let me know.

James B. Peake, M.D.

Attachment

Prepared Statement Paul Seligman, M.D., M.P.H., Associate Director of Safety Policy and Communication, Center for Drug Evaluation and Research, Food and Drug Administration, U.S. Department of Health and Human Services

INTRODUCTION

Mr. Chairman and Members of the Committee, I am Dr. Paul Seligman, Associate Director of Safety Policy and Communication in the Center for Drug Evaluation and Research (CDER) at the Food and Drug Administration (FDA or the Agency), which is part of the Department of Health and Human Services (HHS). I am accompanied today by Dr. Robert Temple, Director of the Office of Medical Policy in CDER. We are pleased to be here today to discuss FDA's role in identifying and communicating about drug safety issues, as well as our role in the protection of human subjects. In my testimony, I will first discuss the importance of FDA drug regulation, including several new initiatives to improve the drug safety system. I will then discuss how the Agency manages drug safety issues and informs the public when drug safety concerns arise. Lastly, I will discuss FDA's role with respect to protection of human subjects.

THE VALUE OF DRUG REGULATION

FDA promotes public health through the regulation of prescription and over-the-counter drugs, which are an increasingly critical component in improving the health of many Americans.

FDA's responsibilities for oversight of the entire life cycle of drugs—from premarket drug testing and development through drug approval, postmarket surveillance, and risk management—have never been more important. FDA continuously seeks to provide the means for translating new scientific advances into benefits for patients (for example, biomarkers and pharmacogenomics), take advantage of new ways to monitor the performance of marketed drugs, and communicate this information to healthcare professionals and patients to help ensure the safe use of drugs.

One aspect of assuring the most appropriate use of marketed drugs is to study them carefully before approval. FDA's drug review process is recognized worldwide as the gold standard, and we actively monitor the scientific bases for our processes to ensure that they reflect advances in medical science. FDA approves drugs after they undergo comprehensive safety evaluations. It is not always recognized, but at least half of the effort by FDA's premarket reviewers is dedicated to the assessment of safety. Major changes have taken place in how drugs are evaluated, including a complete evaluation of their metabolism, their interactions with other drugs, and potential differences of effectiveness or safety in people of different genders, ages, and races. In addition, FDA staff perform systematic assessments of safety that yield comprehensive reviews, focusing on the potential problems with the greatest clinical importance.

The other critical aspect to assuring the most appropriate use of marketed drugs is the process FDA has in place to assess drugs after they are approved. FDA grants approval to drugs after sponsors demonstrate that the drugs meet the Federal Food, Drug, and Cosmetic (FD&C) Act's standard for safety and efficacy. However, no amount of premarket study can provide all of the information about effectiveness or all the risks of a new drug when it is used by the general population in the myriad ways not studied during clinical trials. As a result, FDA's postmarket drug safety program plays an essential role by collecting and assessing information about adverse events and medication errors identified after approval. A key role of our postmarket safety system is to detect serious unexpected adverse events and take definitive action when needed.

NEW INITIATIVES TO IMPROVE DRUG SAFETY

Within the last year, FDA has launched several new initiatives to ensure drug safety. Outlined below are some examples.

Food and Drug Administration Amendments Act of 2007 (FDAAA)

As you know, in September 2007, Congress passed FDAAA, which included new resources for medical product safety and new regulatory tools and authorities to ensure the safe and appropriate use of drugs. For example, under *Title IX—Enhanced Authorities Regarding Postmarket Safety of Drugs,* FDA can require drug sponsors to make certain safety-related labeling changes and conduct postmarketing studies and clinical trials instead of relying on voluntary actions. In addition, under FDAAA, if FDA determines that a risk evaluation and mitigation strategy (REMS) is necessary to ensure that the benefits of a drug outweigh the risks of the drug, FDA can require manufacturers to submit a REMS when a drug comes on the market, or later if FDA becomes aware of new safety data.

Sentinel Initiative

FDAAA requires the HHS Secretary to develop methods to obtain access to disparate data sources and to establish a postmarket risk identification and analysis system to link and analyze healthcare data from multiple sources. On May 22, 2008, FDA launched the Sentinel Initiative with the ultimate goal of creating and implanting the Sentinel System—a national, integrated, electronic system for monitoring medical product safety. The Sentinel System will strengthen FDA's ability to ensure that safe and effective new drugs are available as quickly as possible and that marketed drugs remain safe and of the highest quality.

Action Plan for Import Safety

Another critical aspect to drug regulation is the safety of products imported into the United States. On November 6, 2007, Secretary Leavitt presented to President Bush the "Action Plan for Import Safety" completed by the Interagency Working Group on Import Safety. The Import Action Plan presents broad recommendations and specific short- and long-term action steps, categorized under the organizing principles of prevention, intervention, and response. On July 1, 2008, FDA issued the "Import Safety—Action Plan Update." The update outlines the significant

progress FDA has made and the key steps that are planned for the future to enhance the safety of imported goods. Thus far, FDA has taken strong enforcement actions, signed agreements with key trading partners, hosted bilateral and multilateral discussions, shared critical information on safety and best practices, and began a process to improve safety practices, both inside and outside of government.

Prevention. FDA is seeking to ensure that imported drug products are safe and effective prior to reaching U.S. ports of entry. FDA is pursuing this goal by maximizing foreign product pre-approval inspections, increasing FDA presence in China, increasing FDA inspections, increasing the sharing and use of foreign competent authority inspection reports and other information, developing plans to use third-party certification, and increasing capacity building with countries that have less developed regulatory systems to ensure product safety.

Intervention. FDA recognizes the importance of a strong and effective intervention capacity to identify problems as they occur. FDA has several plans to enhance its Information Technology systems in ways that will enable the Agency to better utilize risk-based information from the entire life cycle of imported products. FDA is expanding laboratory capacity and developing rapid test methods for detection of pathogens and other contaminants in drugs, and ensuring that these test methods are available at ports of entry to assist in determining whether a product should be admitted into the United States. In addition to increasing pre-approval inspections, FDA is increasing surveillance inspections, as well as determining which manufacturing facilities may pose a risk to the American consumer. The Import Action Plan also outlines several action steps intended to help ensure that domestic companies importing foreign source material meet their responsibility to import safe and effective medical products. FDA inspects all facilities listed in a drug application, both foreign and domestic, to determine if they meet the Agency's quality standards. During these inspections, FDA routinely evaluates the domestic drug manufacturer's testing and controls of ingredients (domestic and foreign-sourced) and supplies. If deficiencies are discovered, FDA may take enforcement action.

Response. FDA must be ready to take immediate action when a health threat emerges with any FDA-regulated product. The Import Action Plan calls for increased FDA and U.S. Customs and Border Protection (CBP) cooperation, including developing interdepartmental procedures for clearing and controlling shipments at ports of entry, co-locating FDA and CBP at locations to improve coordination and efficient use of resources, and increasing import information sharing between FDA and CBP through new technology applications. FDA is also working to facilitate the adoption of track-and-trace technologies to identify and track a product along the product life cycle. These technologies will facilitate the timely recovery of the violative product and reduce the opportunity for harm, as well as secure the integrity of the supply chain by providing an "e-pedigree"—an electronic record documenting that the drug was manufactured and distributed under secure conditions.

HOW FDA MANAGES DRUG SAFETY ISSUES

Once FDA approves a drug, the postmarket monitoring stage begins. A drug manufacturer is required to submit regular postmarketing reports to FDA on its drug. These reports include critical information about adverse events associated with the use of one or more drugs. Reports are submitted in an expedited fashion for serious and unexpected risks, and periodically for less urgent safety issues. Manufacturers submit several other types of postmarketing reports, including new clinical trial results. Also during this period, we continuously receive adverse event reports directly from sources, such as healthcare professionals and patients, through our MedWatch program. Stored in a computerized database, these reports are reviewed and analyzed by FDA epidemiologists and safety evaluators to assess the frequency and seriousness of the adverse events and to determine their causes. An adverse event may occur because of simple or complex reasons, including drug exposure, an interaction between one or more drugs, other therapies, environmental factors, an individual's characteristics, and underlying diseases. Our response to information from this ongoing surveillance depends on an evaluation of the aggregate public health benefits of the product compared to its evolving risk profile.

Decisions about regulatory action in response to evidence of a drug safety risk are complex, taking into account many factors. As more becomes known about the potential risks or benefits of a drug, often its FDA-approved labeling will be revised so that it better reflects information on appropriate use. For example, FDA may seek revisions to a drug's labeling to add information on adverse reactions not previously listed, to add new warnings describing conditions under which the drug should not be used, or to add new precautions advising doctors of measures to minimize risk. If labeling alone is inadequate to manage risks, additional actions may include revising drug names or packaging, issuing "Dear Healthcare Professional"

letters (sometimes referred to as "Dear Doctor" letters), educational/special risk communications, requiring restricted distribution programs, or withdrawing a drug's approval.

HOW FDA COMMUNICATES ABOUT DRUG SAFETY ISSUES

FDA uses a broad range of methods to communicate drug safety information to the public. Certain forms of communication are targeted to specific audiences (e.g., healthcare professionals or patients). Others are directed at more than one group to ensure widespread dissemination of information about important drug safety issues, including emerging drug safety issues. FDA continuously evaluates its communication efforts and modifies them to enhance their accessibility and effectiveness. We welcome public comment at any time suggesting ways to improve our safety communications. The different types of drug safety communications are described in more detail below.

Labeling. FDA-approved drug product labeling is the primary source of information about a drug's safety and effectiveness, and it summarizes the essential scientific information needed for the safe and effective use of the drug. Compliance with the recently issued physician labeling rule for prescription drugs is expected to further enhance the usefulness of product labeling and further facilitate the safe and optimal use of prescription drugs.

Labeling for prescription drug products is directed to healthcare professionals but may include patient counseling information as well. For some prescription drugs, such as oral contraceptives and estrogens, FDA determined several years ago that the safe and effective use of these drugs required additional labeling in nontechnical language be distributed directly to patients by their healthcare professional or pharmacist (Title 21 of the *Code of Federal Regulations* (CFR) 310.501 and 310.515). FDA-approved patient labeling also may be provided by manufacturers for other drugs.

Early Communications about Ongoing Safety Reviews. Since August 2007, FDA has issued Early Communications about Ongoing Safety Reviews (ECs) to keep healthcare professionals and the general public informed of postmarket safety issues that are currently being evaluated by FDA. ECs are issued at the beginning of FDA's assessment, prior to conclusive determination of the clinical or public health significance of the information under evaluation and before a decision has been made about what regulatory actions, if any, should be taken. Rather, they reflect FDA's current analysis of available data concerning these drugs, but posting the information as an EC does not mean that FDA has concluded there is a causal relationship between the drug and the emerging safety issue. It also does not mean that FDA is advising healthcare professionals to discontinue prescribing these products. In general, ECs have included a timeframe for when FDA anticipates completing the safety review and providing followup.

Public Health Advisories. FDA issues Public Health Advisories (PHAs) to provide information regarding important public health issues to the general public, including patients and healthcare professionals. For example, PHAs may highlight important safety information, inform the public about the completion of FDA's evaluation of an emerging drug safety issue, announce the implementation of methods to manage the risks identified for a marketed drug, or provide other important public health information.

PHAs regularly include recommendations to mitigate a potential risk and often are issued in conjunction with other drug safety communications, such as Healthcare Professional Sheets. PHAs related to drugs are available through the CDER Web site and disseminated via the MedWatch Partners Program.

Healthcare Professional Sheets. FDA issues Healthcare Professional Sheets, which provide a summary of important and often emerging drug safety information for a particular drug or drug class. Healthcare Professional Sheets begin with a summary "Alert" paragraph, followed by more detailed sections explaining the "Alert," including clinical considerations or recommendations for the healthcare professional, information that patients should be made aware of and discuss with their healthcare professional, a summary of the data that were the basis for the recommendations, and, when applicable, implications of the "Alert."

Healthcare Professional Sheets are intended to provide adequate factual information to address potential questions from patients and facilitate a healthcare professional's consideration of the drug safety issue. As with the PHAs, FDA continues to collect input on the usefulness of these communications through a variety of feedback mechanisms, and anticipates that healthcare professional communications will continue to evolve.

Other Methods of Communication. FDA continues to explore other methods of making its written communications more effective, as well as the use of other media

such as podcasts, video broadcasts and conference calls, to disseminate drug safety information.

Sponsors also use various methods to communicate drug safety information. For example, a sponsor may distribute a "Dear Healthcare Professional" letter to convey important information regarding a marketed drug. "Dear Healthcare Professional" letters may be used to disseminate information regarding a significant hazard to health, announce important changes in product labeling, or emphasize corrections to prescription drug advertising or labeling.

To summarize, FDA has a critical role in the detection and management of safety issues that are identified after a drug is approved, including a critical role in communicating information to the public. The actions taken depend on the characteristics of the adverse events, the frequency of the reports, the seriousness of the diseases or conditions for which the drug provides a benefit, the availability of alternative therapies, and the consequences of not treating the disease. Our goal, regardless of the communication tool employed, is to make the most up-to-date drug safety information available to the public in a timely manner so that healthcare professionals and patients can consider the information when making decisions about medical treatment and be aware of uncertainties in the data. The Agency is committed to providing accurate, clear, reliable, and useful drug safety information.

FDA'S ROLE WITH RESPECT TO PROTECTING HUMAN SUBJECTS

The FD&C Act and its implementing regulations are one part of a complex system of safeguards designed to protect human subjects. Several groups play key roles in the clinical research of products subject to FDA regulation—the company that sponsors the research, the clinical investigator who conducts the research, the Office of Human Research Protection within HHS, when the clinical investigation is federally funded, and the Institutional Review Board (IRB) that has a role in protecting the rights and welfare of the patients who are taking part in clinical investigations. For example, investigators must sign an FDA-Form 1572, committing to comply with their regulatory obligations, and IRBs are subject to detailed rules in 21 CFR part 56. FDA is responsible for regulating the activities of sponsors, investigators, IRBs and others involved in a clinical trial. We take very seriously our role to protect patients enrolled in clinical trials. It should be appreciated, however, that, while a broad set of protections are built into the law and regulations, the professional and ethical conduct of the parties involved in clinical research is crucial to the protection of human subjects.

CONCLUSION

At FDA, assuring the safety and effectiveness of medical products for the American people is one of our core responsibilities. Working with patients, physicians, pharmacists, industry, and State regulators, FDA plays a critical role in the detection and management of drug safety issues, by helping to ensure the safe use of marketed drugs by providing the best possible information to the American public. We also take our role in the protection of human subjects very seriously; working with many other partners to assure that clinical trials are conducted appropriately.

Once again, thank you for the opportunity to testify before the Committee today. We are happy to respond to questions.

Prepared Statement Ponni Subbiah, M.D., M.P.H.,
Vice President, Medical Affairs, Pfizer Inc., New York, NY

Good morning Mr. Chairman, Ranking Member Buyer and Members of the Committee.

My name is Ponni Subbiah. I am a medical doctor and a Vice President in Medical Affairs at Pfizer. I am responsible for the medical and scientific activities for products in the Urology/Respiratory area, which includes Chantix. On behalf of Pfizer, thank you for the opportunity to speak with you today. I would like to briefly address the following areas: the global epidemic of tobacco addiction and its impact on public health; the role of Chantix in helping patients stop smoking; the clinical trial process at Pfizer; how Pfizer monitors drug safety; and, finally, the recent updates to the Chantix label.

The World Health Organization has described tobacco use as the leading preventable cause of death. Worldwide, approximately 1.3 billion people currently smoke cigarettes.[1] In the U.S. alone, more than 438,000 deaths are attributable to smoking each year.[2] More people die from smoking annually than inhabit the city of Miami, Florida.[3] In fact, cigarette smoking is a risk factor for six of the eight leading causes of death in the world—including heart disease, stroke, lung disease such as emphy-

sema, tuberculosis, and lung cancers.[1] Health care costs from smoking-attributable diseases are $75.5 billion annually as per the 2004 Surgeon General's report.[4]

It is important to understand that, for most people, smoking is not a lifestyle choice or habit, but rather an addiction to nicotine. Nicotine is a highly addictive drug—as addictive as heroin or cocaine. Smokers become physically and psychologically dependent on nicotine. Less than 7 percent of smokers are able to quit on their own.[5] Therefore, medications and other therapeutic options are needed to assist smokers who are motivated to quit. Quitting smoking, with or without treatment, is associated with nicotine withdrawal symptoms, which are both physical and mental and may include irritability, anger, depressed mood and weight gain. Quitting smoking has also been associated with the exacerbation of underlying psychiatric illnesses.[6] It is important to assess the benefits and risks of smoking cessation treatments in the context of this setting.

In the United States, currently 20.8 percent of the population in general smoke cigarettes.[7] By comparison the smoking rate in the VA population is 33 percent.[8] Of interest to this hearing, there is a strong link between smoking and a range of psychiatric disorders. A study by Harvard Medical School showed that 35–41 percent of people with mental illness smoke.[9] Smoking prevalence rates are 50–70 percent[10,11] in patients with major depression and over 80 percent in patients with schizophrenia.[11] The smoking rate in post traumatic stress disorder (PTSD) patients ranges from 45–60 percent.[12,13]

Chantix® is the first non-nicotine based medicine developed specifically for smoking cessation and the first prescription aid to smoking cessation approved by the FDA in nearly a decade. It is currently approved in 74 countries and is designed to bind at the same receptor in the brain as nicotine, which allows it to reduce the urge to smoke, while at the same time blocking the effects of nicotine.[14] Chantix® has been demonstrated to be more efficacious than placebo and Zyban (another popular smoking cessation treatment) in two clinical trials. To date, Chantix® has been prescribed to approximately 7.5 million patients worldwide, 5.6 million of those in the U.S.

Chantix® is not a treatment that is used over a prolonged period of time. Rather, physicians should prescribe Chantix® for 3 months for their patients who wish to quit smoking. For those patients who successfully quit with Chantix® by the end of the 3 months, an additional 3 months of Chantix® is recommended to help them remain smoke free.[14]

Chantix® was studied in a comprehensive clinical trial program involving more than 5,000 patients over a span of 10 years. The studies conducted during development of a drug for approval are done in order to fully characterize the unique properties of a medicine. The FDA will approve a medicine for use only when its benefits outweigh the risks. Even after a medicine enters the market, and throughout the lifecycle of the product, Pfizer strives to enhance its knowledge regarding the safety and efficacy of its products through ongoing research in order to continually assess the benefit/risk profile. This includes information not only on risks but also on the important benefits that these medicines may have, especially in specific subpopulations. The benefits and risks that need to be considered will vary between different disease areas as well as between individual patients. Thus, consideration of benefits and risks of medicines is a critical component of the dialog that needs to occur between patients and their doctors.

Gathering data to continuously inform the benefit/risk assessment is accomplished through various means, including conducting clinical trials and epidemiological studies. Gathering this information requires Pfizer to work with outside researchers in a variety of ways such as getting scientific input and involving external experts in Pfizer's clinical study program for a medicine. When clinical trials are conducted, there are various mechanisms in place designed to protect patients from harm. These include independent Institutional Review Boards (IRBs), which are designed to assure that appropriate steps are taken to protect the rights and welfare of patients. Patients must also give their informed consent prior to participating in a study.

Prior to a medicine's approval, Pfizer is the sponsor of, and responsible for, the clinical trials involving the medicine. The company contracts with independent researchers to conduct studies according to international standards and FDA's good clinical trial practice (GCP) regulations. After the medicine is approved, there may be studies done that are not sponsored by Pfizer, but may be supported by the company through the provision of grant funding or free supplies of Pfizer medicines for independent investigator research (IIR) to advance scientific knowledge and understanding. However, Pfizer is not involved in the design, conduct or publication of an IIR study.

There are also clinical trials of Pfizer medicines, such as the trial that is the subject of this hearing, that are conducted independently of Pfizer. Once a medicine is available on the market, any researcher can obtain the medicine and conduct studies without the involvement of Pfizer. These studies may be funded from non-Pfizer sources such as academic institutions or the NIH.

The Pfizer drug safety surveillance system is designed to continuously gather and analyze reports received about patient experiences with our products after they have become available in the market. These adverse event reports are routinely shared with the FDA and other regulators as required. Based on clinical study data and post-marketing reports, we work with regulators on a continuing basis to effectively communicate to patients and healthcare professionals any change in the benefit/risk profiles of our medicines. The primary mechanism of communicating changes in a medicine's benefit/risk profile is the product labeling. It is common for the label to be revised numerous times in a product's lifecycle. In fact, in 2007 there have been over 500 FDA approved safety related labeling changes across various prescription medicines in the U.S. Pfizer's primary goal is to communicate to both physicians and patients what is known about the benefits and risks so that doctors and patients can decide together whether a particular medicine is the best treatment option.

With regard to Chantix®, there have been adverse event reports of certain neuropsychiatric symptoms, including depressed mood, agitation, changes in behavior, thoughts of suicide and suicidal behaviors, in patients attempting to quit smoking with Chantix®. The report of an adverse event does not necessarily mean there is a causal relationship between the product and the event and, in the case of Chantix®, a causal relationship between these reports and the use of Chantix® has not been established. However, in some reports related to Chantix®, a causal relationship could not be excluded. In November 2007 Pfizer worked with the FDA to update the Chantix® label to reflect these reports. Additional label updates were made in January and May 2008, respectively, to put this information in the Warnings section of the label to heighten awareness and to provide further guidance to physicians and patients about these symptoms. The current label advises that a patient should stop taking Chantix® and contact their healthcare provider immediately if agitation, depressed mood, or changes in behavior that are not typical for them are observed or if the patient develops suicidal ideation or behavior.

Pfizer communicated these label updates to physicians, study investigators and other healthcare professionals through various routes including product labeling, written communications, Web site updates (e.g. PfizerPro.com, Chantix.com) and communications from our sales representatives. Patients have access to this information through their healthcare provider as well as through the Chantix® Web site (Chantix.com).

Pfizer reviews the benefit/risk profile of all our products, including Chantix®, on a continuing basis. Based on our review of the available safety information, including the adverse event reports received to date, we believe the Chantix® label accurately reflects the product's efficacy and safety profile, thereby facilitating appropriate use by physicians and patients. In particular, full awareness and understanding by both physicians and patients of the neuropsychiatric symptom related labeling, highlights the key role that doctors and patients can play in managing and mitigating the potential risks, so that the important benefits of Chantix® as an aid to smoking cessation can be realized when appropriate.

There are few things that provide greater health benefits than quitting smoking. Patients who smoke cigarettes should be encouraged to seek support from a healthcare professional and counseled to quit. Health care providers should discuss the risks of smoking, the health benefits of quitting smoking, and the benefits and risks of available treatment options including Chantix®. It has been reported that nearly 70 percent of smokers want to quit, although as indicated earlier, fewer than 7 percent of those who try are able to quit on their own.[5] Given the devastating health effects of smoking, it is essential to have treatment options available to help smokers break free of nicotine addiction and stop smoking.

Thank you. I look forward to answering any questions you may have.

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Prepared Statement John D. Daigh, Jr., M.D., CPA,
Assistant Inspector General for Healthcare Inspections,
Office of Inspector General, U.S. Department of Veterans Affairs

Mr. Chairman and Members of the Committee, thank you for the opportunity to testify today on whether the Veterans Health Administration (VHA), Department of Veterans Affairs (VA), protected human research subjects appropriately following notification from the Food and Drug Administration (FDA) of potentially harmful effects associated with the drug varenicline (Chantix®). Accompanying me today is Dr. Andrea Buck and Mr. Randall Snow.

Chantix® is a medication approved by FDA for use in helping patients to quit smoking. Concerns involving the use of Chantix® escalated following an incident reported in the media in which a veteran taking Chantix® while enrolled in a VHA research study at the Veterans Affairs Medical Center, Washington, DC (VAMCDC) allegedly experienced an episode of agitated and/or aggressive behavior.

To address concerns regarding the use of Chantix®, we focused our review on issues of informed consent, patient notification of potential adverse effects associated with Chantix®, and the tracking and reporting of adverse events occurring during the course of the research study. The scope of our review was limited to the VAMCDC. Our first site visit to VAMCDC was on June 19, 2008. While conducting our inspection, we received allegations of potential inappropriate documentation, which we also reviewed.

The Office of Inspector General initiated this review in response to requests from this Committee and other Members of Congress. My statement today is based on the results of our review, which have been provided to VHA in a draft report for comment. Until we receive VHA's official response and issue the final report, our findings are subject to further clarification.

BACKGROUND

The VHA research study enrolling the veteran compared the effectiveness of smoking cessation treatment administered by mental health providers to that administered by primary care providers in patients with post-traumatic stress disorder (PTSD); it will hereafter be referred to as "the smoking cessation study" or "the study."

The protocol, a written document describing the method for conducting the smoking cessation study, stated that patients assigned to mental health providers for their smoking cessation therapy would receive medications for smoking cessation unless contraindications existed. While Chantix® was not available when this research study began in 2004, the protocol was modified on January 17, 2007, to include circumstances under which Chantix® could be used. Specifically, the protocol

indicated that Chantix® would be provided, "at the discretion of prescribing clinicians for subjects who cannot tolerate or who have failed adequate trials of other smoking cessation medications." Subjects enrolled were required to have the diagnosis of PTSD and to be actively receiving treatment for that disorder. Subjects could not be enrolled if they had a psychotic disorder not in remission, were at imminent risk for suicide or violence, or had severe psychiatric symptoms.

The Cooperative Studies Program (CSP) provided us with a list of 10[1] different VA medical centers which enrolled patients receiving Chantix® in this smoking cessation study. The various sites were overseen by the Cooperative Studies Program (CSP), a VHA program designed to coordinate research occurring at multiple facilities. CSP maintains five coordinating centers, a clinical research pharmacy, four epidemiological research and information centers, and a health economics resource center. The coordinating centers provide statistical and methodological guidance to VA researchers involved in clinical trials. CSP trials have resulted in numerous important contributions to research, including demonstrating the efficacy of a vaccine for shingles and coordinating multiple trials involving cardiovascular treatments that resulted in major innovations in the treatment of hypertension and coronary artery disease.

The research protocol in question utilized the Palo Alto CSP Coordinating Center (the Coordinating Center). The Coordinating Center received all study data from the sites. It forwarded information pertaining to serious adverse events (SAEs) to the Albuquerque Pharmacy Coordinating Center. In an e-mail of June 20, 2008, CSP reported that as of June 18, 2008, there were 158 subjects nationwide who had received Chantix® while enrolled in the research study. This CSP data was based on self-reporting by research subjects during the course of the study. VHA indicated that there is no single data source that can completely and accurately portray actual Chantix® use by those in this study. In addition, VHA reported to us that there was a total of 945 subjects in the study nationwide.

CSP had also reported in the June 20, 2008, e-mail that 11 of the VAMCDC subjects received Chantix®. However, the senior researcher (also known as the senior investigator (SI)) conducting the smoking cessation study at VAMCDC informed us on June 19 (the date of our first onsite visit), that there were a total of 109 subjects in the study at VAMCDC and that 12 of those 109 subjects received Chantix®. Following chart review for these 12 subjects, we found that 1 patient had never actually taken Chantix®. Later, on June 27, 2008, the SI informed us of an additional 4 patients at VAMCDC who received Chantix® at some time during the course of the study; this made a total of 15 patients who received Chantix® as part of this study at VAMCDC. It is these 15 patients whom we discuss throughout this report.

VAMCDC is part of the VA Capitol Health Care Network (Veterans Integrated Service Network (VISN) 5). In addition to acute care services, it maintains a 120 bed long-term care unit and four Community Based Outpatient Clinics. It is affiliated with three medical schools and is a medical readiness partner with three Department of Defense facilities. The VAMCDC also has an active research program, with 70 researchers and 185 active protocols as of June 27, 2008. It also maintains one of two VA War Related Illness and Injury Study Centers.

FDA Notifications Pertaining to Chantix®

The FDA approved Chantix® on May 10, 2006, as an aid for smoking cessation. During pre-marketing studies, more than 4,500 people received Chantix®. Recorded adverse psychiatric reactions included frequent anxiety, depression, emotional disorders, irritability, and restlessness. Initial product labeling did not include any warning regarding any suicidal ideation. VHA added the product to its National Formulary as a third line agent, following failure of nicotine replacement strategies and buproprion, another medication for smoking cessation.

As additional information became available during post-marketing studies, the sponsor modified the patient package insert on November 20, 2007, to include possible adverse reactions such as depression, suicidal thoughts, and agitation. At this time, the FDA issued an "Early Communication About an Ongoing Safety Review" because of post-marketing cases involving suicidal ideation and behavior. This communication specifies that the FDA had not concluded that a causal relationship existed, nor did they advise healthcare professionals to discontinue the product. On January 31, 2008, in response to additional reported adverse events, the FDA requested that all advertising materials be modified to reflect the additional risks. On February 1, 2008, the FDA issued a public health advisory stating that ". . . it ap-

[1] Houston, Hampton, Minneapolis, New Orleans, Philadelphia, Portland, Providence, San Diego, Tuscaloosa, and Washington, DC.

pears increasingly likely that there may be an association between Chantix® and serious neuropsychiatric symptoms."

Human Subjects Protections in Research

Determining if and to what extent this public health advisory altered the relative risks and benefits of the smoking cessation study was the responsibility of the facility's Institutional Review Board (IRB). Each facility in VHA conducting research involving human subjects must have an IRB, which is a Committee vested with the responsibility of protecting human research subjects. The IRB is composed of scientists, physicians, and community members. In the VA, the IRB is a Subcommittee of the Research and Development (R&D) Committee. Any research project must have both IRB and R&D Committee approval.

In research protocols conducted at multiple sites, each site's IRB must approve the protocol, as well as any substantive modifications. In approving the protocol, the IRB must determine that the potential benefits outweigh any risks to subjects involved in the research. Further, the IRB must approve any modifications to informed consent and ensure that each protocol has an adequate plan for monitoring the safety of subjects enrolled in the protocol.

IRBs are required to meet regularly and to maintain minutes of those meetings. They must review all protocols at least annually. IRB Chairpersons may unilaterally approve minor changes to previously approved research using expedited review procedures, providing that the IRB reviews these actions at the next regularly convened meeting.

In addition, IRBs review adverse events (AEs) and serious adverse events (SAEs) occurring during the course of research studies. AEs are defined as "any untoward occurrence (physical, psychological, social, or economic) in a human subject participating in research." SAEs include "death; a life threatening experience; hospitalization (for a person not already hospitalized); prolongation of hospitalization (for a patient already hospitalized); persistent or significant disability or incapacity; congenital anomaly and/or birth defects; or an event that jeopardizes the subject and may require medical or surgical treatment to prevent one."

IRBs do not, however, routinely review files maintained by the researchers, including whether there is a signed informed consent for each research subject. This type of information would be gathered through protocol audits, a process of reviewing the actual implementation of the protocol in accordance with human subjects protections. VHA Directive 2008–014, dated March 12, 2008, mandated that facilities perform such audits. Audit requirements included an evaluation of informed consent. Prior to this Directive, facilities were not required to fully audit research protocols. Rather, IRBs were only required to have a procedure for conducting such audits.

IRBs in VHA are evaluated as part of an accreditation process in VHA. VHA contracted with the Association for the Accreditation of Human Research Protection Programs, Inc. (AAHRPP) to accredit its human subjects protection programs. Accreditation Standards used by AAHRPP include multiple measures of IRB compliance with Federal regulations and VHA policy. They conducted a site visit at the VAMCDC from October 30, 2007–October 31, 2007. Accreditation was not granted. The facility received a status of Accreditation-Pending and was given the opportunity to submit an Improvement Plan.

Scope and Methodology

To address the concerns regarding the use of Chantix® in this research study, we chose to focus our review on issues of informed consent, patient notification of potential adverse effects associated with Chantix®, and the tracking and reporting of adverse events occurring during the course of this research study. The scope of this review is limited to the VAMCDC. Our first site visit to VAMCDC was on June 19, 2008. While conducting our inspection, we received allegations of potential inappropriate documentation, which we also reviewed.

We addressed issues of informed consent by obtaining study records for the research subjects who we were told received Chantix® during the course of the study at VAMCDC. We compared these records to the patients' electronic medical records. As discussed on page 2 of this report, we had identified 15 patients who had received Chantix® at some time during the research. We then attempted to contact 14 of the 15 patients by telephone to determine when and if they had consented to enrollment in a smoking cessation study. As of June 30, 2008, we have been able to speak with 10 of 15 patients; 1 of the 10 was hospitalized and could not be interviewed. An 11th patient was deceased as the result of an unrelated illness. We have called 3 patients whom we have been unable to contact. Therefore, we interviewed 9 of 15, spoke to 1 we could not interview, and were unable to reach 3 of 15; 1 of

15 was deceased as a result of unrelated causes, and 1 we did not attempt to contact.

In addition, we reviewed IRB files, files maintained by the SI at the VAMCDC, e-mail, and pharmacy correspondence pertaining to this protocol. We interviewed the SI, Associate Chief of Staff (ACOS) for Research and Development, the IRB Administrator, study personnel, the research compliance officer, and the Acting Chief of Staff. We obtained and reviewed records from the CSP Coordinating Center in Palo Alto, California, and interviewed staff located at that facility. We reviewed CSP policies and procedures, adverse event reports, and numerous documents from VHA's Office of Research and Development pertaining to the smoking cessation study as conducted by VAMCDC. We also asked the FDA for an opinion regarding whether the November 20, 2007, early communication should have prompted a modification to the protocol. As of the date of this draft, we have not yet received this opinion.

In this report we did not review or comment upon the medical care provided to individual veterans. We reported our findings only in the aggregate form. We performed the inspection in accordance with the Quality Standards for Inspections published by the President's Council on Integrity and Efficiency.

RESULTS

Issue 1: Patient Notification of FDA Communications Concerning Chantix®

The CSP Coordinating Center and the facility's Pharmacy Service appropriately notified providers following the FDA's Early Communication of November 20, 2008. However, following the February 1, 2008, Public Health Advisory, we found that the facility's research service did not ensure that patients involved in the smoking cessation study were notified of the risk of suicidal thoughts or behavior in a timely manner.

The November 20, 2007, Early Communication from FDA

The VAMCDC IRB approved the smoking cessation study on August 16, 2004. The R&D Committee there initially approved the smoking cessation study on August 27, 2004. R&D Committee minutes describe the study as a greater than minimal risk study involving patients with PTSD. The study further required monitoring of PTSD and depression symptoms to determine whether smoking cessation would worsen these conditions.

The IRB re-approved the study under continuing review procedures on July 11, 2005; on May 15, 2006; and on April 9, 2007. The R&D Committee also re-approved the study annually, with the last such approval occurring on April 24, 2008. On April 30, 2007, the IRB approved an amendment to the study, adding Chantix® as a study medication. Further, the consent form was amended to reflect the risks of Chantix® which were known at that time; these included insomnia, unusual dreams, headache, and constipation.

On November 20, 2007, the FDA issued its early communication notifying healthcare professionals of post-marketing cases involving suicidal ideation and occasional suicidal behavior. The Associate Chief of Pharmacy at the facility received this alert the same day via e-mail through a subscription to a service informing healthcare professionals of medication alerts. E-mails describing the risks were sent to providers at the facility on November 21, 2007. The Associate Chief of Pharmacy generated lists of patients by prescriber between November 23, 2007, and November 26, 2007, and indicated that these lists were distributed. They were paper rather than electronic, because all the providers at the facility do not have encrypted e-mail to ensure the privacy and security of the patients' personal information. The Chief of Primary Care confirmed that these lists were distributed.

CSP conducted three conference calls with site researchers between November 20, 2007, and December 31, 2007. The first of these conference calls occurred on November 26, 2007. These minutes record the following statement: ". . . because this is not a drug study, it is not necessary to take action on this [the FDA communication] unless your local IRB requires that you report it to them." On December 3, 2007, minutes reiterate that it was considered the decision of the local IRB as to what actions should be taken following an FDA warning. On December 4, 2007, minutes state the following:

> Given that this is not a drug study and use of varenicline is optional, the Chairs don't feel that sites need to inform their IRBs of this issue unless particular subjects report adverse events related to the medication.

On January 18, 2008, a communication from the VHA Pharmacy Benefits Management Service to healthcare providers stated the following: "FDA's preliminary assessment indicates that many cases presented with new-onset of depressed mood,

suicidal ideation, and behavior and emotional changes within days to weeks of starting varenicline [Chantix®].” Further, the communication described a warning from the European Medicines Agency of suicidal ideation and suicidal attempt in some patients taking Chantix®. The communication recommended that providers “monitor patients taking varenicline for changes in mood and behavior.” We could find no documentation that the SI formally reported this to the IRB, or that the IRB addressed any of the events related to the November 20, 2007, communication. Documentation supplied regarding CSP conference calls between November 20, 2007, and December 31, 2007, make it clear that the CSP believed that local IRBs should decide whether this communication warranted action.

This lack of action is concerning, because it is evident that the pharmacy service considered the November 20, 2007, communication important information requiring dissemination to providers and the creation of lists of patients on this medication. This was particularly important in the smoking cessation study, as it by definition enrolled only those veterans who had PTSD. Because not all the research subjects in the smoking cessation study received their medications from VA providers, and because all providers prescribing Chantix® for patients involved in the study were not listed on the protocol, we were unable to determine by the date of this draft report whether all providers notified patients of these events.

The February 1, 2008, Public Health Advisory

The CSP Coordinating Center and the IRB reacted following FDA’s Public Health Advisory of February 1, 2008. Minutes from a February 5, 2008, conference call between study coordinators and assessment technicians and Coordinating Center staff indicated that the new safety information should be passed along to site clinicians to ensure patient notification. The Human Rights Committee at Palo Alto sent a memorandum to the Director of the Coordinating Center on February 8, 2008. This memorandum stated that, “it is appropriate that veterans who are or who might be prescribed this medication while participating in the study be informed, and given the opportunity to discuss alternative treatments with their provider.” This memorandum also contained the following statement:

> The proposed procedure is that all participants be given the information at their next follow up visit; this will be documented by their signature on the addendum. While this is acceptable for participants who are not receiving the medication, those who are taking varenicline should be notified more urgently.

The CSP Coordinating Center sent a memorandum dated February 13, 2008, to researchers at the VAMCDC stating that patients currently on Chantix® “will receive a copy of the consent addendum in the mail, along with a cover letter explaining the reason for the addendum.” The Center provided a draft of the letter. The letter described risks of “anxiety, nervousness, tension, and depression as well as untoward changes in behavior.” It did not contain any information regarding increased risks of suicidal thoughts or behavior. While the letter did not describe these risks, the informed consent addendum did state that side effects included “thoughts of suicide, and attempted and completed suicide”. However, CSP indicated that patients could sign the addendum at their next study visit. The SI at each site was responsible for ensuring that the letters were sent following IRB approval.

The IRB at VAMCDC subsequently met on March 3, 2008. Minutes from that meeting document that the IRB Chair and Administrator met with the SI on February 29, 2008, to discuss patient notification issues following that advisory. The IRB Chair approved the addendum to the consent form addressing these risks by expedited review on the same day. The SI was to notify all study participants by mail with the letter in addition to the informed consent addendum. The SI planned to notify all study participants, whether or not they were on Chantix®. The minutes include the following sentence: “The FDA states that some patients on varenicline [Chantix®] have an increased risk of depression and suicidality.” Minutes also state that patient notification issues were reported to the research compliance officer for followup.

We interviewed the SI, IRB Administrator, IRB Chair, and study coordinator for the smoking cessation trial at VAMCDC. The IRB Administrator and Chair indicated that it was the SI’s responsibility to actually send the letters. The SI stated the letters were sent to all 109 participants. The study coordinator reported assisting in this task. The letters were not sent with any return receipt requested, or with any other means of verifying delivery to the appropriate individuals. There was no consistent documentation in the electronic medical record that such letters were sent. We interviewed nine of the patients by phone. Three of these patients recalled receiving a letter. The study coordinator indicated that a few letters came back, but

we were unable to locate documentation of any follow-up actions to address these returned letters, or exact numbers of how many were returned.

While we believe these letters were sent, we have no reliable way of determining how many of the veterans actually received notification. Further, we concluded that the letter did not adequately explain the risks associated with Chantix® at that time. We were told that the informed consent addendum was included with the letter when the letters were mailed, but we were unable to find any documentation of sending these items to all affected veterans. Therefore, we found that the notification procedures for patients in the smoking cessation study at the VAMCDC following the February 1, 2008, Public Health Advisory did not adequately ensure that all patients were notified of this risk in a timely manner.

On May 30, 2008, VHA's Pharmacy Benefits Management Service sent an e-mail to VISN formulary leaders and pharmacy chiefs asking them to distribute a letter to veterans taking Chantix® that informed them of the risk of suicide associated with the medication. Two of the six veterans who did not recall receiving the initial letter from the SI recalled getting this letter recently.

While the facility's Pharmacy Service appropriately notified providers of the risks associated with Chantix®, we do not find that the research service ensured that subjects enrolled in the smoking cessation study were notified of these risks. We therefore concluded that the facility notified providers of the adverse effects of Chantix® in an appropriate and timely manner but did not ensure that patients enrolled in the smoking cessation study received this information.

Issue 2: Adequacy of Informed Consent

Federal informed consent regulations govern the use and participation of human subjects in research. The purpose of the regulations is to safeguard the welfare of humans and to assure that the subjects are given enough information about the research so that they may make informed decisions about whether or not to participate.

Patients enrolling in the smoking cessation study were initially required to sign two consent forms. The first indicated the patient's consent to be screened for the study to determine whether they were eligible. If a patient was found eligible for the study, the patient would then sign a second consent form to participate in the research and be informed of any medications which might be used in the study. Over time there were three versions of this second consent form. The first version, we call "the original second consent form." The second version of this form we refer to as the "revised consent form"; it introduced Chantix® to the study and informed the patients of the earliest known risks. The third version of this form we refer to as "the addendum"; it disclosed the greater risks of Chantix® as of February 2008.

Thus, the "original second consent form" to participate in the study contained information pertaining to the risks of nicotine patches, nicotine gum, and buproprion, another medication used for smoking cessation. The original second consent did not contain a mention of Chantix®, which at that time had not yet received FDA approval and was not a part of the research study.

On April 9, 2007, the IRB approved a new second consent form to participate in the study, which is referred to here as the "revised consent" form; it replaced the original second consent. This revised consent form included information on the risks of Chantix® that were known at that time, to include changes in dreams and nausea. We reviewed all the consent forms for all 15 patients identified by the SI as being on Chantix® at some time during the course of the study. We could locate the revised consent form for only 5 of the 15 patients on Chantix®. The SI indicated that patients entering the study after April 9, 2007, were to sign that revised consent form, but that individuals who had already signed the original second consent form were not re-consented during the research study.

Following the February 1, 2008, FDA Advisory, an addendum was created and added to the revised consent form to include information about the risks of suicidal thoughts or behavior for patients taking Chantix®. In this report, we refer to the addendum to the informed consent, which is essentially the third version of the second consent form, as "the addendum." The addendum was initially approved through expedited review on February 29, 2008, and disclosed that Chantix® could cause "changes in behavior, anxiety, nervousness, tension, depression, thoughts of suicide, and attempted or completed suicide." The SI stated that she mailed the addendum to all patients within the study, not just to those on Chantix®. On April 1, 2008, minutes from a CSP conference call between study personnel and the Coordinating Center indicated that the study coordinator and assessment technician from the VAMCDC site reported that "a number of patients have signed the consent addendum."

Chantix® next appears in the VAMCDC IRB minutes of May 5, 2008. These minutes document a discussion between a patient who experienced an episode of aberrant behavior while on Chantix® and the SI and the Chief of Psychiatry. The patient wanted to withdraw from the study and a letter to that effect was signed by these parties and witnessed by the IRB Chair. On May 6, 2008, another CSP conference call occurred in which VAMCDC study personnel stated that they were "actively approaching subjects about the varenicline (Chantix®) addendum and obtaining signatures."

We reviewed only those charts of the 15 patients identified as having taking Chantix® at some time during the course of the review. We could locate signed addendums including information about the risks of suicidal thoughts or behavior for only 6 of these 15 patients as of June 23, 2008. Of these 6, only 2 were signed prior to June 20, 2008. We do note that, of the patients without a signed addendum in their chart, one had died as the result of an unrelated illness and another had moved out of the area. Medical records demonstrate that 11 of the 15 patients had visited the medical center between March 3, 2008, and June 20, 2008.

Despite evidence that study personnel at the VAMCDC reported that the consent process was going well on numerous occasions, we found that the facility failed to obtain patient signatures on the addendum to the informed consent describing the risk of suicidal thoughts in patients taking Chantix®. Patients also were not re-consented with the April 9, 2007, consent form, which added Chantix® to the list of medications already utilized by study prescribers and disclosed risks known to be associated with the drug at that time. Minutes from a June 2, 2008, conference call between CSP and research personnel at the VAMCDC once again record that VAMCDC told the CSP that "[T]he varenicline [Chantix®] consent process is going well."

Further, we found that the facility's research compliance program failed to appropriately monitor the adequacy of the informed consent process at the facility. The research compliance officer obtained her current position in October of 2007. Since that time, she told us she has "been in training mode." She reviewed the consent forms for this study but did so only from the perspective of whether the informed consent process was documented appropriately. She did not verify that there were consents for all patients enrolled in this study. AAHRPP noted several deficiencies relating to the informed consent process in its October 2007 visit. Standards described as "NOT MET" by AAHRPP included:

1. Researchers "develop an informed consent process and method of documentation appropriate to the type of research and the study population, emphasizing the importance of participant comprehension and voluntary participation."
2. The Research Review Unit has and follows "written policies and procedures requiring that the investigator has and follows a procedure for properly documenting informed consent."
3. The Research Review Unit "reviews the content of the consent process including the consent document, and the process through which informed consent is obtained from each participant, focusing on measures to improve patient understanding and voluntary decisionmaking."

We do note, however, that the facility did not receive a copy of the Final Site Visit Report from AAHRPP until March 19, 2008. AAHRPP did not accredit the VAMCDC; rather, they gave it a status of Accreditation Pending. An Improvement Plan is due to AAHRPP on July 14, 2008.

Issue 3: Psychiatric AEs and SAEs in Patients Enrolled in the Smoking Cessation Study Receiving Chantix®

We also reviewed whether the VAMCDC appropriately monitored AEs and SAEs occurring during the course of the smoking cessation study. Our review of SAEs was limited to psychiatric events occurring at the VAMCDC in patients who had taken Chantix® at some time during the course of the study. We did not evaluate all adverse events from the VAMCDC or SAEs from any of the other sites.

At the VAMCDC, we found reports for 4 SAEs relating to psychiatric hospitalizations for 3 of the 15 patients; 1 of those patients was on Chantix® at the time. Three SAEs were dated in early 2007; the fourth was in early 2008.

We then sought to determine whether the Coordinating Center had evaluated the communications from FDA in terms of the study results nationwide. We did find that they considered this problem. They initially decided not to change reporting requirements of AEs following the November 20, 2007, communication. Prior to the February 1, 2008, warning, sites were required to report SAEs but not all AEs. However, following the February 1 warning, sites were required to report AEs and SAEs. The Data and Safety Monitoring Board for the nationwide Chantix® study

met on February 27, 2008. Minutes from this meeting contain the following statements:

> [A Board member] reported that the number of SAEs [includes all SAEs, not just psychiatric SAEs] continues to be high. Often one or two life-threatening events are reported in a day, but most are not study related... The study chose to include varenicline [Chantix®] when it became available. [The Board member] noted that the original [market-related] studies [on Chantix®] did not include people with active mental disorders, so we are starting to see the affect [sic] now in our population. We are asking sites to report these side effects on the SAE forms even if they are only AEs [adverse events].

Also on February 27, 2008, the human rights Committee at the CSP Coordinating Center in Palo Alto met and discussed Chantix®. Minutes reflect a discussion of the fact that the initial Chantix® studies evaluating its safety did not include subjects with comorbid mental health diagnoses. Minutes state that the "study Co-Chairs agreed to check with sites and review how those participants who are taking varenicline, but are not in therapy, are being monitored." We were not provided with any written documentation regarding if or when this occurred.

Study results provided to us described 25 serious adverse events of a psychiatric nature which occurred while patients were enrolled in the study nationwide. This did not mean that these events were related to the study or that they occurred while the patient was actually taking Chantix®. By definition, all patients in the study had pre-existing mental illness. The 25 events disclosed included 16 patients with suicidal ideation; 1 who attempted suicide; and 1 who had homicidal thoughts.

We are concerned, however, by the comment in the Data Safety and Monitoring Board minutes stating that we are seeing the effects now "in our population." This made the human rights Committee decision to review how patients taking Chantix® were to be monitored all the more important. However, we do note that data provided reflected that only a single possible Chantix®-related event occurred during the course of this study nationwide. Interpreting nationwide data for this study, however, is expressly beyond the scope of this review.

Issue 4: Alleged Documentation Irregularities in the Smoking Cessation Study at VAMCDC

During the course of our review, we received allegations that study personnel had falsified certain study records at VAMCDC. The smoking cessation study required study personnel to fill out a number of written documents based upon direct patient interviews. One such document was the Clinician Administered PTSD Scale (CAPS) form. This is a structured interview used in part to assess the severity of PTSD symptoms in study participants. At VAMCDC the study coordinator could not complete this form because he was not a clinician. The assessment technician typically completed these forms at the VAMCDC.

On June 24, 2008, the ACOS for R&D notified ORO of allegations he received regarding inappropriate documentation of information contained on the CAPS form for two patients associated with the smoking cessation study. It was reported that the study coordinator completed these forms based on information contained in other documents, rather than from a direct patient interview.

We reviewed the CAPS forms, and interviewed the study coordinator. We were unable to interview the assessment technician because of reported health problems. The study coordinator admitted that in two instances, he completed these forms from information obtained from other forms. He further stated that he had the assessment technician on the telephone who offered advice as to how to complete these forms. We verified that in at least one of these instances, the assessment technician was on leave without pay on the day of the patient's visit.

Based upon this information, we conclude that the CAPS form in at least one instance was not completed by a clinician during a direct patient interview as required by the protocol. Further, we were told that this particular record was faxed to the Coordinating Center along with the other data collected at this site. We therefore found that this employee did not complete the form in accordance with the protocol, and we question the accuracy of the data contained on that form.

In addition, we reviewed quality control reports sent from the Coordinating Center concerning their evaluation of study data submitted from the VAMCDC. These reports were provided on a weekly basis. The Coordinating Center reports contain numerous entries concerning VAMCDC's missing pages, missing data, and inconsistent data. While data entry errors are exceedingly common, we are concerned about these reports in light of the information described above.

CONCLUSION

The actions of study personnel regarding the completion of the smoking cessation study records suggest that the accuracy of such records may be in dispute. Data used in the type of important trials described in this report may be used to define the standard of care for PTSD patients who want to stop smoking. The quality control reports reflect that CSP monitored data submissions regularly. However, the Coordinating Center could not be expected to detect whether the CAPS form was appropriately completed from a direct patient interview or extrapolated from other study data. These kinds of documentation irregularities may affect the credibility of study results. While in this case we have no reason to believe that the problem is not remediable, it reinforces the need for monitoring of data collection and researcher records at a local level.

The human rights Committee at the Coordinating Center suggested special monitoring for study subjects taking Chantix® and not receiving therapy. We were not able to locate documentary evidence that this recommendation was ever implemented at VAMCDC. Further, the VAMCDC did not initially supply us with an accurate number of patients having ever taken Chantix® during the course of the study, suggesting that local sites may not have been tracking which patients were and were not taking Chantix®. This makes it unlikely that they ever identified the subgroup of those patients who were not actively receiving therapy while taking Chantix®.

In addition, the absence of signed informed consent addendums describing the effects of Chantix® after they were known to researchers at the VAMCDC is also of concern. While the SI at the VAMCDC did send out a letter in late February or early March 2008 to at least some participants in the study, we have no documentary evidence of who received it or when. This prevents us from ensuring that patients were notified in a timely fashion once side effects of Chantix® were known. We also did not find that the letter contained sufficient warning regarding the possible risk of suicidal thoughts or actions, but note that this information was in the enclosed addendum to the consent form.

We also found that the pharmacy service provided timely notification to clinical care providers, including lists of patients on the medication. The VA sent letters dated May 30, 2008, to identified patients on Chantix® to alert them to medication side effects. We believe that this was sufficient for the general population of patients in the facility taking Chantix®. However, research subjects, who by definition had active PTSD, represented a group uniquely susceptible to neuropsychiatric side effects. We believe that the Coordinating Center recognized this in deciding to modify the informed consent and mail letters to patients. The local implementation of this directive, however, is at issue in that the VAMCDC did not ensure that these patients signed informed consent addendums or received letters notifying them of the additional risks.

Finally, the deficiencies involving informed consent identified in the AAHRPP review suggest that the VAMCDC may not be adequately monitoring the informed consent process on a systemic scale. The scope of this review prevents us from making a definitive statement with regard to the VAMCDC's research program overall, but deficiencies identified in the AAHRPP report suggest that some issues may be systemic in nature. Therefore, we make the following recommendations:

RECOMMENDATIONS

1. The Under Secretary for Health will ensure that all patients who currently take Chantix® have been informed of the possible association between Chantix® and suicidal thoughts.
2. The Under Secretary for Health will develop a formal mechanism for ensuring that Institutional Review Boards are directly notified of FDA communications concerning medications when they are responsible for protocols involving those medications.
3. The Under Secretary for Health will ensure that all patients involved in the smoking cessation study are informed of the risks associated with Chantix® by VHA study personnel and given the opportunity to sign the addendum to the informed consent disclosing those risks.
4. The Under Secretary for Health will take appropriate administrative action, to include a research misconduct inquiry, based upon the findings contained within this report.
5. The VISN 5 Director will require that the smoking cessation study data collected at VAMC Washington, DC, be validated to ensure its accuracy.
6. The VISN 5 Director will require the medical center director to audit a representative sample of all active protocols involving human subjects for compli-

ance with VHA informed consent requirements, including whether an informed consent can be located for each study participant.

7. The VISN 5 Director will require the medical center director to ensure that protocols are being audited in accordance with VHA Directive 2008–014.

Mr. Chairman, in closing, I would like to once again thank you and the other Members of the Committee for the opportunity to testify on this important matter. Dr. Buck, Mr. Snow, and I would be pleased to answer any questions.

Statement of Gerald P. Koocher, Ph.D., Professor and Dean, School of Health Sciences, Simmons College, Boston, MA

Mr. Chairman,

I welcome the opportunity to appear before the Committee today in an effort to provide information that may prove useful to the Members and staff as you seek answers to questions about ethical standards in the design and execution of behavioral and bio-medical research with vulnerable human participants.

The central ethical concerns in any research involving people should focus on their informed participation and safety. The first ethical cornerstone involves an individual's consent to participate. Often called "informed consent," the concept involves providing information by its very definition. The key elements to consent include:

- Access to all of the information that might reasonably influence one's willingness to participate;
- Adequate knowledge and understanding of that information, and
- Voluntariness and freedom from coercion in the decision to participate or withdraw from participation.

Obtaining consent does involve documentation, but is best conceptualized as a process by which the investigator makes certain that potential participants know what will be asked of them, what risks or hazards may be involved, what benefits may result. In addition, the consent process must inform participants about their right to withdraw at any time, and provide contact information for responsible parties in the event of any problems or complaints. Those providing this information have the obligation to communicate these details in language the participants can understand. If the investigator plans changes to a project after obtaining consent, the process must be reinitiated with the new details provided and agreed to by participants.

Many research projects involve studying healthy people. However, most research populations of interest and available to mental health professionals are restricted or vulnerable in ways that may not allow a full measure of self-determination. From the standpoint of this Committee's concerns, such populations may include people at high risk for some possibly preventable outcome, disabled individuals, and those who may face social or economic disadvantage. Some potential participants may have additional vulnerabilities because of their mental or emotional condition, such as anxiety, depression, or symptoms of post-traumatic stress. Other vulnerabilities may arise from physical illness or issues of confidentiality that bear on social stigma or discrimination.

In addition to adhering to legal regulations, the ethical obligation to protect all research participants rests with the investigators, who stand accountable to professional codes of ethics and a number of regulatory bodies including Institutional Review Boards (IRBs), Data Safety Monitoring Boards (DSMBs), and federal agencies such as the Food and Drug Administration (FDA). Both IRBs and DSMBs include independent content area experts and representatives of the public. IRBs and DSMBs typically review research plans, eligibility or exclusion criteria, consent forms, data analysis/management protocols, and adverse events (generally characterized as AEs, adverse events, or SAEs—serious adverse events, as when a death occurs). Any changes in research protocols that might bear on the safety of participants require advance approval by the institutional IRBs, and DSMBs in the case of multi-site trials. All of these processes and safeguards generally involve substantial documentation.

In certain exceptional circumstances an IRB may waive obtaining written consent. For example, suppose an investigator seeks anonymous survey data via the Internet or unobtrusively observes the public behavior of anonymous people in everyday settings (e.g., recording how often many people line up at the "8 items or less" supermarket checkout counter with more than 8 items). In such circumstances an IRB would typically waive the requirement of individual consent. Even in such instances, however, the investigator would formally request the waiver and the IRB would document granting it.

As a person who has served as a principal investigator, as an IRB member, as a current DSMB member for the N.I.M.H., and who has studied IRBs and research integrity, I hope that I can provide the Committee with information that will assist you in reviewing the research projects of concern to you.

MATERIAL SUBMITTED FOR THE RECORD

110TH CONGRESS
A
RESOLUTION
OFFERED BY MR. FILNER

Be it resolved by the Committee on Veterans' Affairs, that the Democratic Membership of the standing Subcommittee of the Committee for the 110th Congress shall be as follows:

Subcommittee on Health
Michael H. Michaud, Maine, Chairman

Corrine Brown, Florida
Vic Snyder, Arkansas
Phil Hare, Illinois
Shelley Berkley, Nevada
John T. Salazar, Colorado
Donald J. Cazayoux, Jr., Louisiana

"VA Testing Drugs on War Veterans, Experiments Raise Ethical Questions"
The Washington Times
By Audrey Hudson
June 17, 2008

The government is testing drugs with severe side effects like psychosis and suicidal behavior on hundreds of military veterans, using small cash payments to attract patients into medical experiments that often target distressed soldiers returning from Iraq and Afghanistan, a *Washington Times*/*ABC News* investigation has found.

In one such experiment involving the controversial anti-smoking drug Chantix, the Department of Veterans Affairs (VA) took 3 months to alert its patients about severe mental side effects. The warning did not arrive until after one of the veterans taking the drug had suffered a psychotic episode that ended in a near lethal confrontation with police.

James Elliott, a decorated Army sharpshooter who suffers from post-traumatic stress disorder (PTSD) after serving 15 months in Iraq, was confused and psychotic when he was Tasered by police in February as he reached for a concealed handgun when officers responded to a 911 call at his Maryland home.

Mr. Elliott, a chain smoker, began taking Chantix last fall as part of a VA experiment that specifically targeted veterans with PTSD, opting to collect 30 a month for enrolling in the clinical trial because he needed cash as he returned to school. He soon began suffering hallucinations and suicidal thoughts, unaware that the new drug he was taking could have caused them.

Just 2 weeks after Mr. Elliott began taking Chantix in November, the VA learned from the Food and Drug Administration (FDA) that the drug was linked to a large number of hallucinations, suicide attempts and psychotic behavior. But the VA did not alert Mr. Elliott before his own episode in February.

In failing to do so, Mr. Elliott said, the VA treated him like a "disposable hero."

"You're a lab rat for $30 a month," Mr. Elliott said.

One of the Nation's premier medical ethicists said the VA's behavior in the anti-smoking study violated basic protections for humans in medical experiments.

"When you're taking advantage of a very vulnerable population, people who have served the country, and the agency that's responsible for their welfare isn't putting their welfare first, that's a pretty serious breach of ethics," said Arthur Caplan, director of the Center for Bioethics at the University of Pennsylvania.

In all, nearly 1,000 veterans with PTSD were enrolled in the study to test different methods of ending smoking, with 143 using Chantix. Twenty-one veterans reported adverse effects from the drug, including one who suffered suicidal thoughts, the 3-month investigation by *The Times* and *ABC News* found.

Mr. Caplan, who reviewed the consent and notification forms for the study at the request of *The Times* and *ABC News*, said the VA deserved an "F" and that it has an obligation to end the study, given the vulnerability of veterans with PTSD and the known side effects of Chantix. "Continuing it doesn't make any ethical sense," he said.

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The VA continues to test Chantix on veterans, even as reported problems with the drug increase and have prompted at least one other federal agency to take action. On May 21, the Federal Aviation Administration banned airline pilots and air traffic control personnel from taking Chantix, citing the adverse side effects.

The VA responds

VA officials defend their use of veterans in medical studies, saying that helping PTSD sufferers to stop smoking would prolong their lives. As for the three-month delay in notifying its patients about the Chantix problems, the VA said bureaucracy slowed down their warning because the alert letters had to be issued through an Institutional Review Board (IRB) that oversees the experiment at each VA location.

"We don't have the authority to just send directly to patients material that has not been approved by the IRB sites," said Miles McFall, director of the VA's programs for PTSD sufferers. "We did sense urgency. And we respond to that urgency doing just what we did here, which was, I think, incredibly quick response for a governmental institution.

"We believe that we took responsible action by informing the clinicians who are the people most in touch with the patients to be on the lookout for any potential side effects and to respond appropriately," he said.

While Mr. Elliott blames Chantix for his mental breakdown and confrontation with police, VA officials said they cannot be sure.

"We don't know that Chantix was the cause of this, first of all. And it's presumed that that's the case. We don't know that to be a fact," Mr. McFall said.

Mr. McFall said the veterans with PTSD in the anti-smoking study "are at high risk to use tobacco" and the goal of the experiment is to determine how best to deliver treatment—through a mental health counselor or a smoking clinic. Chantix was one of several options tested on the veterans.

"FDA approved, and that drug is available to help individuals stop smoking and VA makes that drug available," Mr. McFall said. "It does not deny access to them."

Asked about adverse reactions now linked to the drug, Mr. McFall said: "We are certainly aware of FDA warnings and we took all precautions. . . . so it can be used safely. All drugs have side effects or potential side effects."

Dark history of medical tests

The government has a controversial history of using military personnel as human research subjects.

Mustard gas was tested on the military during World War II, radiation during the early Cold War period, LSD in the sixties, herbicide in Vietnam and Panama, and chemical and biological warfare drugs during the Gulf War, according to Senate testimony given by the Vietnam Veterans of America (VVA) on July 10, 2002.

In most of those cases, few if any military test subjects were informed of the potential health consequences of the exposure.

"We have a phrase to describe this phenomenon—the disposable soldier syndrome," said Richard Weidman, former VVA director of government relations.

The most infamous government experiment is the Tuskegee Syphilis Study conducted by the U.S. Public Health Service from 1932 through 1972, which used 400 poor and uneducated black male sharecroppers who carried the sexually transmitted disease.

The men were purposely undiagnosed and untreated for a disease that already had progressed to late stages, and were studied through autopsy.

The government effectively blocked the unwitting participants, who also were drafted in 1940 to serve in WWII, from receiving medical treatment for symptoms they were told were caused by "bad blood." Of the participants, 28 men died of the disease, 100 others died from complications brought on by syphilis, and the disease spread to 40 wives and 19 children.

Ongoing tests with vets

The VA has extensive screening of veterans who enroll in medical experiments and requires detailed consent forms to ensure patients know about the potential complications and benefits.

Currently, the VA and other federal agencies are conducting nearly 300 clinical studies involving veterans with PTSD. Most studies are behavioral, including one that tests the effects of yoga on PTSD sufferers.

Twenty-five, however, are testing drugs on 4,796 veterans, more than half (2,488) of whom are just returning from the wars in Iraq and Afghanistan, according to clinical trials filed with the National Institutes of Health (NIH) and reviewed by The Times.

One study conducted by the National Institute of Mental Health is using virtual-reality exposure—sights, sounds and smells from the Iraq battlefield, along with a drug called D-Cycloserine that reduces fear.

Other studies are testing drugs on veterans with PTSD, including the antidepressants paroxetine, mirtazapine and citalopram—all carry warnings of suicidal side effects.

"Over 150,000 soldiers are currently deployed in Iraq as part of Operation Iraqi Freedom (OIF) and 12 percent of returning OIF veterans have PTSD," said one study that is using the drug paroxetine on 160 veterans "who have returned from the Iraq theater within the past six months."

Warnings about taking paroxetine include "suicidal thinking about harming or killing oneself or planning to trying to do so" among young adults up to 24 years of age, according to NIH.

Another study on the use of mirtazapine for veterans of Iraq and Afghanistan is testing the efficacy and tolerability of the drug on 100 veterans. Citalopram is being tested on 300 veterans "exposed to high levels of combat stress."

The NIH warning for paroxetine also applies to mirtazapine and citalopram.

The VA has not revealed how many veterans are registered in an experiment to study the effects of divalproex in the treatment of PTSD, but the FDA warned health care professionals on Jan. 31 it had received reports of suicide and suicidal thoughts linked to the anticonvulsant drug.

Smoking study's fine print

Mr. Elliott was one of 940 veterans with PTSD who participated in the Veterans Affairs Cooperative Studies Program (CSP) # 519, "smoking-cessation treatment for veterans with post traumatic stress disorder" ongoing at 10 VA clinics.

The CSP studies date back to the 1940s, when 10,000 veterans suffering from tuberculosis were recruited into VA studies to test different drugs to treat the disease.

The smoking-cessation study uses nicotine replacement products like gum and patches as well as Chantix—a drug that is supposed to block certain brain receptors that make smoking pleasurable. The $11 million taxpayer-funded study was approved in 2004, two years before the FDA approved Chantix for prescription use.

The FDA says that nearly 40 suicides and more than 400 incidents of suicidal behavior have since been linked to Chantix.

Mr. Elliott began taking Chantix on Nov. 6. Two weeks later, on Nov. 20, the FDA issued its first alert that it had "received reports of suicidal thoughts and aggressive and erratic behavior in patients who have taken Chantix," also known as varenicline.

"A preliminary assessment reveals that many of the cases reflect new-onset of depressed mood, suicidal ideation, and changes in emotion and behavior within days to weeks of initiating Chantix treatment," the November FDA alert said.

"The role of Chantix in these cases is not clear because smoking cessation, with or without treatment, is associated with nicotine withdrawal symptoms and has also been associated with the exacerbation of underlying psychiatric illness. However, not all patients described in these cases had pre-existing psychiatric illness and not all had discontinued smoking," the FDA said.

On Jan. 18, the drug manufacturer Pfizer revised its warning label to state "patients who are attempting to quit smoking with Chantix should be observed for serious neuropsychiatric symptoms, including changes in behavior, agitation, depressed mood, suicidal ideation and suicidal behavior."

On Feb. 1, the FDA held a news conference to announce that new health risks have been associated with the drug.

VA officials started addressing the FDA alert on Nov. 26 and Dec. 4 with conference calls among government officials "to inform prescribers about these potential problems and advise patients accordingly," according to a timeline agency officials provided The Times.

On Feb. 4, VA officials were told to "formulate and approve an action plan," and on Feb. 13, a second consent form and letter was submitted for approval by VA officials.

The letter received by Mr. Elliott and other veterans was dated Feb. 29, more than three weeks after he already had suffered his mental breakdown and confrontation with police.

VA letter watered down?

While the alerts from Pfizer and the FDA clearly mentioned suicide and suicidal thoughts as possible side effects, the VA's letter to its veterans used no such language.

"Scientists have recently learned that varenicline can sometimes have serious side effects in some people," the VA letter said. "These side effects may include an increase in psychiatric symptoms such as anxiety, nervousness, tension and depression as well as untoward changes in behavior."

Asked why the letter omitted the most significant side effect, Mr. McFall said "the more verbiage you use, the more difficult and lengthy it becomes, hard to read. It's more likely veterans won't pay attention to it if you overdo."

However, a secondary research consent form sent with the letter that participants are now being asked to sign cites "changes in behavior, anxiety, nervousness, tension, depression, thoughts of suicide, and attempted and completed suicide."

Mr. McFall said the serious side effects were included in the secondary consent form, and not the notification letter, because "it's better to have the letter be brief" so that it is not a "burden for people who sometimes have problems reading."

"They have eyesight problems," Mr. McFall said. "Many of our veterans are getting elderly, so we're trying to keep things simple and to the point, while at the same time pointing them to the most important document, which is the consent form."

Veterans who are participating in the smoking-cessation program are carefully screened to ensure they are not suicidal, psychotic or homicidal, Mr. McFall said.

According to the VA research consent form Mr. Elliott initially signed, he would be required to fill out questionnaires "about some war zone events that you may have experienced" and interviews "regarding symptoms of other psychiatric disorders and your use of drugs and alcohol."

"Has there been a time in the past month when things were so bad that you were thinking a lot about death or that you would be better off dead?" is one example question listed on the consent form.

Mr. Elliott filled out monthly checklists on the extent to which he had nightmares about his military experience or flashbacks, became "super alert" or on guard, and whether he had a "feeling as if your future will somehow be cut short."

Chantix debate

New York Magazine writer Derek De Koff detailed the nightmares and suicidal behavior he suffered while on Chantix in a Feb. 10 article, and said that at one point he felt like throwing himself in front of a tour bus or crashing his head into a computer screen.

"All this seemed logical, but also weirdly funny, even at the time: I could see how crazy these impulses were, I could recognize them as suicidal cliches. But I couldn't make them go away," Mr. De Koff wrote.

In September, musician Jeffrey Carter Albrecht was shot by a neighbor who mistook him for a burglar. The guitarist and keyboardist who once played with Edie Brickell & New Bohemians went on a rant that friends say was fueled by alcohol and the drug Chantix.

A spokesman for Pfizer could not be reached after three calls seeking comment. However, in full-page ads published May 29 in several newspapers including U.S.A. Today, Dr. Joseph Feczko, Pfizer chief medical officer, said the company is "committed to patient safety" and "furthering our knowledge of Chantix."

The FDA has declined to pull Chantix from the market, citing the health benefits of smoking cessation.

"This actually is a very important drug," Dr. Celia Winchell, team leader for the FDA division of anesthesia, analgesia and rheumatology, said during the February teleconference announcing the new warning.

"Although we are getting these reports, there's also a lot of anecdotal reports out there where this drug has worked when no other drug would," Dr. Winchell said.

"Smoking itself has very serious consequences. And so I think it's important to try to manage the risk associated with the drug, also realizing that it has a lot of benefits for some folks," Dr. Winchell said.

More than 5,000 people were treated with the drug in preliminary trials before it was approved for prescription use. However, patients with serious psychiatric illness such as schizophrenia, bipolar disorder and major depressive disorder did not participate in those tests.

Ethics of future VA tests

Mr. Caplan, the bioethicist, said that using veterans with PTSD in clinical trials carries a "high risk" that must be addressed by the VA.

"Researchers have a special obligation to vets with PTSD since they are a vulnerable population somewhat prone to threats or even violence against themselves or others," he said. "They need to keep a hawk-like eye on subjects involved in high

stress experiments and make sure that families and friends are involved and on board any research projects to help monitor subjects."

"I am not against research to try and improve the health of those with PTSD but only if it is done with the highest levels of consent, transparency, supervision and accountability," he said.

Mr. Caplan recommended several steps the government should adopt before allowing future testing on vulnerable veterans, including more participation by families and veterans on Committees that review and approve research proposals.

Future studies that involve veterans with PTSD also should receive special approval from the VA secretary.

And a clear policy should be established that prohibits drugs reported to have serious side effects be tested on populations at risk of those side effects, including veterans with PTSD, he said.

"Congress Demands VA Investigation, Obama, Pelosi, Others Hit Drug Testing"

The Washington Times

By Audrey Hudson and S.A. Miller

June 18, 2008

Democratic presidential candidate Sen. Barack Obama and congressional leaders on both sides of the aisle Tuesday called for investigations into the Department of Veterans Affairs (VA) failure to inform in a timely manner veterans participating in medical tests that a drug they were taking has side effects that can lead to psychosis and suicide.

Responding to an investigative report published in *The Washington Times*, Tuesday, Mr. Obama, a member of the Senate Committee on Veterans' Affairs, said the VA's actions in sponsoring the drug tests were "outrageous" and "unacceptable."

"Our veterans—particularly those suffering from mental health injuries—should have the very best healthcare and support in the world, they should never be needlessly exposed to drugs without proper notification of the dangers involved or effective monitoring of the side effects," said Mr. Obama, Illinois Democrat.

Rep. Steve Buyer of Indiana, the ranking Republican on the House Committee on Veterans' Affairs, sent a letter to the VA inspector general and the VA's chief research and development officer requesting an investigation.

"I am troubled by allegations that these safeguards may have not been in place for this study and I am requesting an immediate investigation into this matter and I asked that VA report back to me as soon as possible," he said.

A spokesman for House Speaker Nancy Pelosi, California Democrat, said Congress also will look into the matter.

"This report raises many disturbing questions about the treatment of our veterans and the House Veterans' Affairs Committee will get to the bottom of this," said Pelosi spokesman Nadeam Elshami. "We expect full and immediate cooperation from the VA."

The VA took three months to notify its patients about severe mental side effects of the anti-smoking drug Chantix, after the Food and Drug Administration issued an alert about side effects that could lead to psychosis and suicide.

The VA said notification letters were tied up in bureaucracy, but thought the three-month timeframe was not unrealistic. The VA also said warnings about suicide were omitted from the letter notification because many veterans are elderly or have eyesight problems.

"This is the most pathetic excuse that can be dredged up; it's insulting," retired Marine Lt. Col. Roger Charles, editor of *DefenseWatch*, the Internet newsmagazine of Soldiers for the Truth, said Tuesday.

"And then to brag you got it done in three months because of a cumbersome bureaucracy? What if people's lives were at risk? Oh wait, they are," Col. Charles said.

The VA continues to test Chantix on veterans suffering from post-traumatic stress disorder (PTSD), even as the Federal Aviation Administration has banned airline pilots and air traffic control personnel from taking the drug, citing the adverse side effects.

Arthur Caplan, one of the nation's premier medical ethicists, said the VA's behavior in the anti-smoking study violated basic protections for humans in medical experiments, *The Times* reported.

The White House on Tuesday defended the VA, saying the program is designed to help soldiers with PTSD.

"The VA is doing everything they can to be mindful of the safety of these veterans in all their programs and try to help them. This is the [VA], under wonderful leader-

ship by [Secretary James B. Peake], who is interested in the health and safety of these veterans that are under his care, and every other member of that VA system is the same," White House spokesman Tony Fratto said.

"These are people who care for our veterans. They care for the troops that have been out there every day, fighting for this country. And they're interested in their safety," he said. "Remember, this is a program dealing with former soldiers with PTSD. And it's a smoking-cessation program. And they're interested in helping these veterans. So that's my reaction to it."

Nearly 1,000 veterans with PTSD were enrolled in the VA study to test methods of ending smoking, with 143 using Chantix. Twenty-one veterans reported adverse effects from the drug, including one who suffered suicidal thoughts, a three-month investigation by *The Times* and *ABC News* found.

"I was very concerned to read this morning's *Washington Times* and learn that the Department of Veterans Affairs (VA) has yet again failed to take appropriate steps to safeguard the health and well-being of veterans participating in drug trials," Mr. Obama said in a letter Tuesday to Mr. Peake.

Mr. Obama cited a Government Accountability Office investigation of VA healthcare in Los Angeles that resulted in the suspension of all human testing because of numerous problems, including "failures to provide adequate information to subjects before they participated in research."

"Accordingly, I call on you to conduct a full and thorough investigation of the process by which VA conducts clinical trials and to take immediate corrective action to address the problems that were first identified by GAO 8 years ago," he said in the letter.

Sen. John Cornyn, Texas Republican and a member of the Senate Armed Services Committee, also requested that Mr. Peake review the studies and identify everyone involved, as well as provide care "to any veterans who have undergone this testing and ensure that any unethical practices are immediately brought to a halt."

"Our wounded troops and veterans deserve the very best in care, but unfortunately, recent studies and incidents illustrate that some VA services have failed to live up to the standard of excellence that is expected," Mr. Cornyn said.

In addition, Senate Veterans' Affairs Committee Chairman Daniel K. Akaka said his panel will question the ethics of the clinical trial involving the drug Chantix.

"The suggestion that VA researchers are not properly informing veterans about possible risks is troubling and deserves further investigation," the Hawaii Democrat said.

Sen. Richard M. Burr of North Carolina, ranking Republican on the Veterans' Affairs Committee, also is questioning the VA clinical trial—in particular the timing of notification to study participants.

"VA should make every effort to quickly inform participants of any new drug information," Burr spokesman Mark Williams said.

Added Kevin Bishop, spokesman for Sen. Lindsay Graham, South Carolina Republican: "Advances in medicine should not come at the expense of our troops."

Stephen Dinan and Jon Ward contributed to this report.

"Veterans as 'Lab Rats'"
The Washington Times Editorial
June 18, 2008

It's time that the House and Senate Committee chairs investigate the Department of Veterans Affairs for medical ethics. As a three-month *Washington Times*/*ABC News* investigation revealed Tuesday, the VA is testing drugs with sometimes-severe side effects on hundreds of military veterans, including many post-traumatic stress syndrome patients, in trials whose risks the participants may not fully recognize. Evidence of troublingly slow risk assessment and predatory-sounding enticements for Iraq and Afghanistan veterans are the chief shortcomings that beg Galen's principle: "First, do no harm." The lives of service-member participants are too important, and the integrity of government post-traumatic stress disorder research is too vital, for the federal government to be taking these manifest risks.

The scope of the problem is potentially very large, even systemic. The federal government has conducted 25 drug tests on veterans with post-traumatic stress disorder and carried out 300 studies on the disorder itself. (An estimated 300,000 Iran and Afghanistan veterans suffer from the disorder or from depression.) There are at least five test drugs bearing warnings about suicide or suicidal thoughts. Also, 4,796 military veterans are enrolled in post-traumatic stress disorder studies—including 940 in the smoking cessation study that raised red flags. One hundred forty-three veterans in this study take Chantix, which is made by Pfizer Inc. and is the

drug-cessation drug under special scrutiny in *The Washington Times*/ABC News investigation. The potential side effects of Chantix include neuropsychiatric symptoms, such as suicidal thoughts and depressed mood. Twenty-one veterans have reported adverse side effects because of Chantix—and the drug is still being used in VA studies.

"Lab rat" is how one Iraq veteran describes his experience in the VA's volunteer medical experiments—and little wonder. Former Army sharpshooter James Elliott of Silver Spring was not informed of the serious potential side effects of Chantix until after a post-traumatic stress disorder recurrence that resulted in a potentially lethal encounter with police. The Iraq veteran assumed the study would follow safe protocols when he signed up for a chance to quit his habit of three packs of cigarettes a day and to receive the $30 monthly enticement. But soon, his nightmares and stress reactions returned with suicidal thoughts, to the point that his fiancé called the police fearing Mr. Elliott might hurt himself. In the resulting standoff, police Tasered the armed Mr. Elliott, who recollects in an interview: "I would have shot me."

Why was a distressed veteran, who served 15 months in Iraq, not informed of Chantix's serious potential side effects until after this potentially lethal encounter?

Chantix was a moving target, but the federal government was much too slow to respond. In November, the Food and Drug Administration (FDA) issued its first warning about Chantix. On Jan. 18, Pfizer updated its warning label: "[P]atients who are attempting to quit smoking with Chantix should be observed for serious neuropsychiatry symptoms, including changes in behavior, agitation, depressed mood, suicidal ideation and suicidal behavior." Yet it was not until Feb. 29 that the VA wrote to veterans and issued its own warning about "untoward changes in behavior" and side effects, including "anxiety, nervousness, tension, depression, thoughts of suicide, and attempted and completed suicide."

According to the FDA, nearly 40 suicides and more than 400 incidents of suicidal behavior have been linked to Chantix. But it took three months for the Chantix warning to make its way through the VA system and to the patients, as this week's *Washington Times*/*ABC News* study showed. It was during that time Mr. Elliott relapsed into post-traumatic stress.

Too many lives were put at unnecessary risk—veterans' lives and those of neighbors, family and law enforcers—in a pattern that could easily recur unless and until the VA is better managed. At the very least, the VA should end the trials of Chantix.

The lax communications regarding the Chantix trials are unconscionable. The federal government can do better: It must do better.

The changes coming to bear at institutions like Walter Reed Army Medical Center and VA medical facilities are welcome. But human life is more important. This is a prime opportunity for those in Congress who strive for improved oversight of the executive branch. James Elliott's story is not one the government should allow to be repeated.

"VA Reports More Chantix Effects,
Study Participants Had 26 'Serious' Events"
The Washington Times
By Audrey Hudson and Amy Fagan
June 19, 2008

War veterans with post-traumatic stress disorder suffered a total of 26 serious adverse events while participating in a Veterans Affairs study of the anti-smoking drug Chantix, a VA official said Wednesday night.

"Based on current data 26 Serious Adverse Events (SAE) occurred in patients while on Chantix," VA spokesman Matt Smith said in a statement e-mailed to *The Washington Times*, adding that 10 of the adverse events "were of a psychiatric nature."

His e-mail also said, under a listing of "Adverse Events," that there were two cases of suicidal thoughts.

The agency previously said that 21 adverse events, only one of them serious (a case of suicidal thoughts), were recorded in the study that uses a drug now linked to psychotic and suicidal behavior, the details of which were reported in an exclusive *Washington Times*/*ABC News* investigation this week.

Mr. Smith said officials could not determine whether the drug study is linked to the side effects.

"Causality can only be determined at the conclusion of a study when there are sufficient data available for analysis," he said.

House Veterans' Affairs Committee Chairman Bob Filner, with other Democrats on his panel, sent a letter Wednesday to VA Secretary James B. Peake requesting immediate response to dozens of questions about his agency's treatment of servicemembers in its medical studies. The letter was issued before the agency released the new numbers.

Mr. Smith said the new numbers are based on "additional data" that has accumulated since the agency spoke to *The Times* on May 21.

"A single patient can have more than one event—a breakdown patient by patient is not available," Mr. Smith said.

Citing the investigative report, the congressmen inquired about how the VA informs participants involved in drug studies about possible side effects and whether the agency terminates studies that use drugs after the Food and Drug Administration (FDA) has issued alerts about them.

"This report raises serious questions about how the VA and FDA coordinate their studies, and how the VA responds to FDA post-approval alerts, particularly when vulnerable segments of the veteran population are involved in the studies," Mr. Filner, California Democrat, and fellow Democratic Reps. Edward J. Markey of Massachusetts and Paul W. Hodes of New Hampshire, said in their letter.

The Times and *ABC News* first reported on Tuesday that a VA-sponsored smoking-cessation experiment on nearly 1,000 veterans suffering from post-traumatic stress disorder (PTSD) provided the drug Chantix to 143 participants.

The drug testing began in January 2007, and the FDA issued its first alert about dangerous side effects to Chantix in November. The VA did not warn its participants taking Chantix until 3 months later.

Earlier Wednesday, Mr. Filner demanded that the VA immediately terminate experiments in which a drug now linked to psychotic and suicidal behavior is being administered to soldiers suffering from PTSD.

"The VA must immediately suspend this study until a comprehensive review of the safety of the protocol is conducted," he said.

"Once the FDA issued the warning that it had received reports linking Chantix to suicidal thoughts and aggressive and erratic behavior, the VA should have immediately suspended this study and notified participants of the possible dangers. Instead, the VA took more than 3 months to notify patients and they did so in bureaucratese that did not clearly state the side effects of the drug."

Mr. Filner also announced that he will hold hearings in early July "to figure out why it took so long to notify patients of the side effects of the drug that was used in this study."

The VA warning was issued too late for James Elliott, a decorated Army marksman who suffered a psychotic episode that ended in a nearly fatal confrontation with police. Mr. Elliott said the VA treated him as a "disposable hero."

According to the FDA, nearly 40 suicides and more than 400 incidents of suicidal behavior have been linked to Chantix. Yet the VA has continued the study and administered Chantix to veterans with PTSD.

Arthur Caplan, one of the Nation's premier medical ethicists, said the VA's behavior in the anti-smoking study violated basic protections for humans in medical experiments, *The Times* reported.

On Tuesday, presumptive Democratic presidential candidate Sen. Barack Obama and congressional leaders on both sides of the aisle called for investigations into the VA's failure to inform in a timely manner veterans participating in the medical tests.

Rep. Steve Buyer of Indiana, the ranking Republican on the House Veterans' Affairs Committee, sent a letter to the VA inspector general and the VA's chief research and development officer requesting an investigation. A spokesman for House Speaker Nancy Pelosi, California Democrat, also said Congress also will look into the matter.

The White House on Tuesday said that the VA is doing everything it can to be mindful of the safety of these veterans in all its programs and try to help them.

"These are people who care for our veterans. They care for the troops that have been out there every day, fighting for this country. And they're interested in their safety," White House spokesman Tony Fratto said.

On Wednesday afternoon, Mr. Filner told *The Times*' "Inside the Story" radio program that Mr. Elliott's story "speaks volume."

"This is the bureaucratic dynamic in all its glory," Mr. Filner said.

Mr. Elliott praised the medical treatment he has received from his doctors at the VA but said human testing belongs in the private sector.

"I don't lambaste the VA as a whole," he said. "They have treated me well, the prosthetics department, my primary care doctor, a lot of people work very, very hard and they themselves are veterans and they do care."

"It's just sad the psychiatric department has bought into human research. The VA should never conduct human research. They should be there to treat veterans' existing problems. Advancing healthcare should not be at the cost of men and women in the military," Mr. Elliott said.

"Doctors Raised Chantix Worries Last Year, Quiet Investigation Preceded Warnings by Months"
The Washington Times
By Audrey Hudson and Amy Fagan
July 8, 2008

Department of Veterans Affairs doctors began raising red flags last year about whether the smoking-cessation drug Chantix was causing severe psychotic episodes among veterans, prompting a quiet investigation last fall but no warning for many months to the 32,000 retired servicemembers prescribed the medication, according to internal agency documents reviewed by *The Washington Times*.

"Early reports" from doctors at VA medical centers were flowing in throughout 2007, well before the U.S. Government and drug maker Pfizer Inc. issued public warnings late last year and earlier this year that Chantix had been linked to psychotic behavior, hallucinations and suicides, VA officials said.

By late November, VA officials began collecting data showing nearly one out of every 1,000 veterans taking the drug had been hospitalized for severe psychosis, a rate noticeably higher than for veterans trying to stop smoking with alternative treatments like nicotine replacement, the documents show.

VA officials told *The Times* that they decided to proceed with their normal process of studying their data for several months to determine whether the trend was "statistically significant" and did not issue immediate warnings.

In the interim, more veterans were prescribed the drug, including some suffering from post-traumatic stress disorder (PTSD) who were enrolled in a medical experiment in which VA officials acknowledged Monday that the number of severe side affects averaged nearly one problem for every two veterans taking Chantix. VA officials said they wished in retrospect that their warnings had been issued sooner and they are examining how to improve their communications process.

The House Veterans' Affairs Committee is set to investigate the VA's conduct in prescribing Chantix at hearings Wednesday, and the Committee's chairman said Monday that the inaction detailed in the documents obtained by *The Times* raised serious, new questions about whether the agency cared enough about the veterans it treats.

"When questioned, the VA immediately wants to defend 'the process,'" said Rep. Bob Filner, California Democrat. "When is the VA going to understand that it is not about the process, but about the veteran? Veterans don't want to hear the VA defend its process. It's time for the VA to defend our veterans, our heroes."

Doctors treating veterans were reporting last year into a medical surveillance database maintained by the VA numerous instances in which the patients were taking Chantix when they were hospitalized for serious psychotic episodes. By October, the VA changed its tracking of Chantix side effects to include psychosis because of the concerns raised by doctors. A month later, the VA began a formal review that took nearly 4 months to complete, gleaning from the database all reports of psychotic behavior that required hospitalization.

That review found that among 27 patients taking Chantix who were admitted to VA hospitals for psychiatric problems since the drug was approved for the market in 2006, 11 had attempted suicide, one attempted homicide, nine had suicidal thoughts, and six were suffering from hallucinations, according to an internal report completed on March 18.

Results "show a greater crude rate of severe psychosis with varenicline compared to nicotine or nicotine/bupropion but do not reach statistical significance," the report concluded. "These data show a signal for potential increased psychosis and warrant further examination to determine actual incidence and potential causality compared to control."

The study was never released to the public, but VA officials agreed to let *The Times* review it.

The VA internal analysis examined more than 100 hospitalizations for psychiatric episodes of VA patients who had just begun trying to quit smoking by taking either varenicline (Chantix), nicotine-replacement therapy, or nicotine-replacement therapy along with bupropion. It looked back at the time period between September 2006 and September 2007.

VA officials noted that patients in the other groups also were admitted to hospitals for similar episodes, including 73 veterans who were trying the nicotine-replacement therapy and seven who were trying nicotine-replacement therapy and bupropion.

But the rates of these events were highest among the Chantix group—9.8 hospitalizations per 10,000 patients. For instance, veterans taking nicotine replacement were suffering psychotic episodes requiring hospitalizations at a lesser of rate 6.8 per 10,000 patients.

The report also found that nearly all of the patients in each of the three groups who were admitted to hospitals with psychiatric problems had histories of psychiatric problems, and more than half in each group had histories of some sorts of suicidal behaviors.

By the time the review was completed in March, the Food and Drug Administration (FDA) and Pfizer already had issued public warnings about Chantix.

Even then, VA officials conducting the review didn't urge that all veterans taking the medicine under the VA's care get warning letters. Instead, the review recommended that the FDA conduct a full epidemiological study of the drug at a cost of $250,000.

Virginia Torrise, VA's deputy chief consultant of Pharmacy Benefits Management, said agency officials were not able in their informal review "to actually correlate and say there was a causal effect" between any of the drugs or nicotine treatments and the psychiatric events and that is why they recommended a formal FDA study.

The VA began sending warning letters to all 32,000 veterans who have taken Chantix in late spring, nearly 3 months after the internal review was completed. The first letters were sent on May 30 and told veterans that they should be careful operating heavy machinery if they are taking Chantix, repeating a warning just days earlier from the Federal Aviation Administration when it banned pilots from taking the drug.

Updated guidelines for prescribing Chantix were posted on the VA Web site June 18, and the agency then sent out letters to all veterans taking the drug to specifically warn them that suicidal tendencies were a possible side effect.

Those actions were prompted by a joint investigative report by *The Times* and *ABC News* on June 17 that documented how the VA failed to warn more than 200 veterans suffering from PTSD who where participating in a smoking-cessation study of Chantix's possible side effects. During the delay, one of the Iraq War veterans, former Army sharpshooter James Elliott, in that study suffered a psychotic episode so severe that it led to a near lethal confrontation with police, *The Times* reported.

The VA initially reported that 143 veterans had taken Chantix in conjunction with the smoking-cessation study, and about two dozen had suffered some side effects. But on Monday, VA officials significantly raised those numbers, acknowledging that at least 241 veterans in the study had taken Chantix as of June 25, and that 114 serious adverse events were reported by 75 of those participants. Among the side effects, 22 involved psychiatric events.

The number of veterans now taking Chantix in that study has dropped to 40, officials said.

The description of the study's effort provided to *The Times* said that when the FDA approved Chantix, "the drug had not been studied in VA patients or patients with mental health conditions."

"VA received early reports of . . . adverse drug reactions from various medical centers which signaled to VA the need for a pharmacovigilance effort that added psychosis to the events being tracked and ultimately analyzed and placed into a report," the VA said.

Wednesday's congressional hearing will review the VA process for handling human research subjects, the agency's responsibility to respond to the FDA's advisories, and the relationship between pharmaceutical companies and researchers. Witnesses include VA Secretary James B. Peake; Dr. John D. Daigh, assistant inspector general; Mr. Elliott; and Lt. Col Roger Charles, editor of *DefenseWatch*.

Lawmakers are concerned because the VA's alerts about Chantix side effects lagged those of the drug maker and the FDA.

For instance, Pfizer updated its Chantix label in January to warn of possible "serious neuropsychiatric symptoms, including changes in behavior, agitation, depressed mood, suicidal ideation and suicidal behavior."

The FDA first issued a notice about possible additional side effects of Chantix in November and issued a health alert on Feb. 1, warning that Chantix could result in changes in behavior, agitation, depressed mood, suicidal thoughts and attempted suicide.

U.S. Department of Veterans Affairs
Assistant Secretary for Congressional and Legislative Affairs
Washington, DC.
July 18, 2008

The Honorable Bob Filner
Chairman
Committee on Veterans' Affairs
U.S. House of Representatives
Washington, DC 20515

Dear Mr. Chairman:

As promised by the Secretary of the Department of Veterans Affairs during the House Veterans Affair's Committee hearing on July 9, 2008, enclosed is the response to Congresswoman Shelley Berkley's inquiry about a veteran testifying that he had unsuccessfully sought emergency care at the Washington DC Veterans Affairs Medical Center. This response is the result of the findings of the Office of Medical Inspector.

Please note that the enclosure contains individually identified personal information which is protected by the Privacy Act, 5 U.S.C. § 552a, the Veterans Records Confidentiality Statute, 38 U.S.C. § 5701 (a), 38 U.S.C. § 7332, and the HIPAA Privacy Rule, 45 C.F.R. Parts 160 and 164. Each of these authorities limits the Department's ability to publicly disclose the information in an individually identifiable form. While this information is not protected by these authorities once under the Committee's jurisdiction, it is considered to be of a sensitive nature. You may wish to consider this fact in any decision whether to redisclose this information. In order to protect the personal privacy of individuals who may be identified from the records provided to the Committee, the Committee may wish to delete any identifying personal information before redisclosing these records. If the Committee wishes, the Department would be pleased to assist by providing a suitably redacted copy for public release.

As the Secretary has said many times, trust, accuracy and transparency are paramount to maintaining the Department of Veterans Affairs' relationships with our veteran patients, with you and other Members of Congress.

Sincerely yours,

Christine O. Hill
Acting Assistant Secretary

Attachment:
"Quality of Care Concern—Veterans Integrated Service Network 5 Veterans Affairs Medical Center Washington, DC," Interim Report 2008—D-963, Office of the Medical Inspector, Veterans Health Administration, U.S. Veterans Administration, July 18, 2008. [The attached report will be retained in the Committee files due to confidential personal information included in the report.]

Committee on Veterans' Affairs
Washington, DC.
July 14, 2008

James Elliott
407 Thayer Place
Silver Spring, MD 20910

Dear James:

In reference to our Full Committee hearing "Why Does the VA Continue to Give a Suicide-Inducing Drug to Veterans with PTSD?" on July 9, 2008, I would appreciate it if you could answer the enclosed hearing questions by the close of business on August 20, 2008.

In an effort to reduce printing costs, the Committee on Veterans' Affairs, in cooperation with the Joint Committee on Printing, is implementing some formatting changes for materials for all full committee and subcommittee hearings. Therefore, it would be appreciated if you could provide your answers consecutively and single-spaced. In addition, please restate the question in its entirety before the answer.

Due to the delay in receiving mail, please provide your response to Debbie Smith by fax at 202–225–2034. If you have any questions, please call 202–225–9756.

Sincerely,

BOB FILNER
Chairman

QUESTIONS FOR THE RECORD

Questions from the Honorable Bob Filner
For James G. Elliott
Before the Committee on Veterans' Affairs Hearing
"Why Does the VA Continue to Give a
Suicide-Inducing Drug to Veterans with PTSD?"
July 9, 2008

Question 1: From what I understand, the primary objective of the study was to compare the effectiveness of two approaches for delivering smoking cessation treatment for veterans with PTSD. The first approach was offering smoking cessation treatment in conjunction with mental health care for PTSD and the second approach was referral to specialized smoking cessation clinics (VA's usual standard of care). This study was not a drug trail or investigation into the effectiveness of Chantix®. Was this your understanding of the study you were enrolled in? If no, please explain what you thought was the purpose of the study?

Response: The use of oral medications was never mentioned to me until 30 October, 2007. In the initial 3-hour meeting with Mary Ann Rapp and Lloyd Webster, I was told that the study was to last three years and that it would in conjunction with my mental health care. I was told that Dr. Hallie Lightdale would prescribe me nicotine patches. I was told that they were not concerned about short term results.

Question 2: According to the VA, Chantix® is meant to be used as a third option for those who fail to quit smoking by nicotine replacement therapy and Zyban (buproprion). Were you given any other smoking cessation drugs prior to Chantix®?

Response: No, I was never offered any other pharmaceutical options other than Varenicline Tartrate/Chantix®."

Question 3: You mentioned in your written testimony that you began to suffer serious dermatological side effects by the time you started taking the full dosage regimen for Chantix®. As a result, you quit taking the medicine until you were told to resume by your prescribing physician. From the time you initially took Chantix® to the time you quit, due to the dermatologic side effects, did you experience any other side effects, such as anxiety, nervousness, tension, depressed mood, unusual behaviors or suicidal ideation?

Response: Yes. I began having extreme nightmares, paranoia and began calling in air strikes at night in my sleep.

Question 3a: When you were told to resume Chantix® by your physician, were you informed of the possible side effects listed in the FDA Early Communication?

Response: I was not informed of the possible side effects listed in the FDA early communication when Dr. Lightdale told me to resume taking Varenicline Tartrate/Chantix®.

Question 4: In November, the FDA issued an Early Communication saying that it had received reports of suicidal thoughts and aggressive and erratic behavior in patients who have taken Chantix®. If the VA had told you these were possible side effects of Chantix®, would you have requested to be withdrawn from the study or considered using another smoking cessation drug?

Response: If the VA had told me of those possible side effects I would not have continued taking Varenicline Tartrate/Chantix® and would have withdrawn from the study.

Committee on Veterans' Affairs
Washington, DC.
July 14, 2008

Lieutenant Colonel Roger Charles, USMC (Ret.)
Vice-Chairman, Soldiers For The Truth
Editor, DefenseWatch
2605 Russell Road
Alexandria, VA 22301

Dear Roger:

In reference to our Full Committee hearing "Why Does the VA Continue to Give a Suicide-Inducing Drug to Veterans with PTSD?" on July 9, 2008, I would appreciate it if you could answer the enclosed hearing questions by the close of business on August 20, 2008.

In an effort to reduce printing costs, the Committee on Veterans' Affairs, in cooperation with the Joint Committee on Printing, is implementing some formatting

changes for materials for all full committee and subcommittee hearings. Therefore, it would be appreciated if you could provide your answers consecutively and single-spaced. In addition, please restate the question in its entirety before the answer.

Due to the delay in receiving mail, please provide your response to Debbie Smith by fax at 202–225–2034. If you have any questions, please call 202–225–9756.

Sincerely,

BOB FILNER
Chairman

Questions for the Record
Questions from the Honorable Bob Filner
For Lieutenant Colonel Roger G. Charles, USMC (Ret.)
Vice-Chairman, Board of Trustees, and Editor
DefenseWatch
Before the Committee on Veteran's Affairs Hearing
"Why Does the VA Continue to Give a
Suicide-Inducing Drug to Veterans with PTSD?"
July 9, 2008

Question 1: Could you tell this Committee your experience with Mr. Elliot and how you got involved with the veteran?

Response: Mr. Elliott and his fiancé, Ms. Hilburn, contacted Eilhys England Hackworth, Chairperson of SFTT's Board of Trustees. Ms. England told me to check into the merits of their story and provided me contact information on Mr. Elliott and Ms. Hilburn. I initially met with Ms. Hilburn, and subsequently with both her and Mr. Elliott. After validating the essential elements of the information they provided, I decided that Mr. Elliott's story deserved wider attention than what my posting a story in our cyber-based newsletter, *DefenseWatch*, could provide.

I then contacted the Executive Editor of the *Washington Times*, Mr. John Solomon, and provided him my assessment that this was a significant news story. He put me in contact with a member of his staff, Ms. Audrey Hudson, who took the story for further action.

Question 2: While writing the story, did you interview or talk with any of the VA staff regarding Mr. Elliott? If so, could you tell us what type of reaction you received from the staff?

Response: I did not contact the VA staff regarding Mr. Elliott.

Committee on Veterans' Affairs
Washington, DC.
July 14, 2008

The Honorable James B. Peake, M.D.
The Secretary
Department of Veterans Affairs
810 Vermont Avenue, NW
Washington, DC 20420

Dear Mr. Secretary:

In reference to our Full Committee hearing "Why Does the VA Continue to Give a Suicide-Inducing Drug to Veterans with PTSD?" on July 9, 2008, I would appreciate it if you could answer the enclosed hearing questions by the close of business on August 20, 2008.

In an effort to reduce printing costs, the Committee on Veterans' Affairs, in cooperation with the Joint Committee on Printing, is implementing some formatting changes for materials for all full committee and subcommittee hearings. Therefore, it would be appreciated if you could provide your answers consecutively and single-spaced. In addition, please restate the question in its entirety before the answer.

Due to the delay in receiving mail, please provide your response to Debbie Smith by fax at 202–225–2034. If you have any questions, please call 202–225–9756.

Sincerely,

BOB FILNER
Chairman

Questions from the Honorable Bob Filner, Chairman,
House Committee on Veterans' Affairs
July 9, 2008
Why Does the VA Continue to Give a Suicide-Inducing Drug to Veterans with PTSD?

Question 1: This incident is merely the latest incident in a series of events, from the suicides in Dallas to the e-mail suggesting VA providers downgrade the diagnosis of PTSD to "adjustment disorders" to the e-mail downplaying the epidemic of suicides in the VA that have caused this Committee to question the VA's accountability measures. What actions do you plan on taking to address what seemingly are process issues and communications problems within the VA?

Response: The Department of Veterans Affairs (VA) clinical response to new information about varenicline demonstrates effective and responsible action. On November 21, 2007, one day after the Food and Drug Administration (FDA) issued an *Early Communication* about possible psychiatric side effects of varenicline, VA's pharmacy benefits management (PBM) program distributed this information to pharmacists and providers throughout the system. Notification of patients through their physicians, who prescribed the medication, started happening almost immediately. Warning labels affixed to every prescription for varenicline were changed in December 2007 to advise patients to, "Call your doctor immediately if you experience mood changes, such as new or worsening feelings of sadness, depression, or fear."

On January 18, 2008, VA issued further guidelines based on new information received from the European Medicines Agency (EMEA) and FDA stating, "Health care providers should educate veterans prior to starting varenicline about the possibility of changes in behavior or mood and that the veteran should report any changes of behavior or mood to the provider. Health care providers should monitor veterans taking varenicline for changes in mood and behavior." This guidance also noted both EMEA's preliminary warning about the risk of suicidal ideation and suicide attempt within the context of smoking cessation attempts and FDA's preliminary assessment of additional cases of suicidal ideation and depressed mood for those taking varenicline. After the FDA issued a *Public Health Advisory* on February 1, 2008, VA notified clinicians on February 5 and called specific attention to the risk of suicidal ideation.

After FDA changed labeling on the medication on May 16, 2008, VA issued a national Bulletin (May 30) to all practitioners informing them of the new warnings, and also sent a patient letter for formulary leaders and pharmacy chiefs to provide to their patients.

In addition, following the recent news reports, VA sent a letter on June 20 to all patients using varenicline, asking them to contact VA if they experience any changes in mood or behavior or thoughts of suicide, and offering to find another way to help them quit smoking.

Within the context of VA's research program and cooperative studies program (CSP) study number 519, on June 25, 2008, the Secretary of Veterans Affairs directed the Under Secretary for Health to conduct four evaluations:

1. The Secretary requested a comprehensive review of CSP–519, through VA's Office of Research Oversight (ORO). These results and an action plan with recommendations were presented to the Secretary on August 11, 2008.
2. Despite the fact that CSP–519 is not a drug study, the Secretary directed that there be Institutional Review Board (IRB) reviews of all post traumatic stress disorder (PTSD) drug protocols in our system to ensure that there is appropriate sensitivity to the study population in the context of FDA alerts and warnings. The Secretary also directed a review of the risks of medications that are likely to be used in the study population and the proper subject notification of associated risks. With ORO to report results to the Secretary, and the Under Secretary for Health to provide an action plan on September 5, 2008.
3. The Secretary tasked Office of Research and Development (ORD) and the Office of Pharmacy Benefits Management (PBM) to conduct a review of VA's adverse event reporting system to ensure that there is, in fact, timely reporting and analysis of data, and that the system supports the appropriate escalation of reporting and sensitive issues for subject safety. The Veterans Health Administration (VHA) presented these results and action plan to the Secretary on July 29, 2008.
4. The Secretary required PBM to review VHA's medication notification policies to ensure the system's support timely communications to patients and providers, including those in research programs. Results and action plan were reported to the Secretary on July 29, 2008.

In addition, the Inspector General investigated human subject protections in CSP–519 at the Washington, DC VA Medical Center (VAMC). The Office of the Inspector General has discussed its findings with the Secretary and prepared its draft report.

VA recently created a central IRB to enhance the efficiency of IRB review of multi-site research projects, including the review and approval of notices to be sent to research participants (for example, new information about the project, changes in the protocol and/or informed consent).

Question 2(a): On February 13, the Cooperative Studies Program (CSP) sent a consent addendum and a letter to each of the Institutional Review Boards (IRBs) at the 11 different sites to serve as a baseline for notification to all study participants. The IRB at the Washington, DC VAMC approved the letter and consent addendum on March 3, 2008, a reasonable turnaround time. However, IRB approval at Houston did not occur till April 30, in New Orleans it did not occur till May 28, and in Portland it did not occur till June 13. In April 2008, there were 42 study participants on Chantix® between the Houston, New Orleans and Portland sites. This was nearly one-third of the total study participants taking Chantix®. Don't you think that IRB approval for the consent addendum and letter was much too slow at these sites?

Response: VA is concerned about the time that elapsed at a number of study sites between the receipt of the letters and consent addendums by IRBs and when they were received by veterans, as well as the lack of follow-up by study coordinators to ensure that their directions were carried out. There is a clear need for improvement in these areas. VA is conducting several investigations into these research practices and has recently created a central IRB to enhance the efficiency of IRB review of multi-site research projects, including the review and approval of notices to be sent to research participants.

Question 2(b): Who is responsible for ensuring that each site's IRB approves the consent addendum and letter in a timely manner?

Response: The Chair(s) of the IRB are responsible for ensuring each site's IRB approves the consent addendum and letter in a timely manner. The facility director is ultimately responsible for ensuring the integrity of the program. In CSP–519, the timing of mailings of the letter and the consent form addendum were left to the individual IRBs. VA's agreement with study participants indicated that if any new specific information became available related to the study we would inform them, and study leaders determined that the FDA's *Public Health Advisory* (dated February 5, 2008) met that standard.

Question 2(c): What is reasonable turn around time for IRBs to approve and send the letters to study participants?

Response: Each IRB decides when and how to approve any consent addendum or letters. However, VA is conducting investigations into these research practices and has created a central IRB to enhance the efficiency of IRB review of multi-site research projects, including the review and approval of notices to be sent to research participants (such as new information about the project, changes in the protocol and/or informed consent).

The Secretary directed the Under Secretary for Health to conduct a review of the risks of medications that are likely to be used in the PTSD study population and that there is proper notification to research participants of associated risks. The ORO is to report their findings to the Secretary, and the Under Secretary for Health will provide an action plan on September 5, 2008.

IRBs are established by the Federal Policy (Common Rule) for the Protection of Human Subjects at 38 CFR Part 16 and by FDA regulations at 21 CFR Part 56 and all processes for reviews and approvals are the responsibility of the respective IRB. With regard to reasonable turnaround times, these vary according to the circumstances of the study and the seriousness of the new information. For example, an FDA or manufacturer recall would demand immediate notification of all affected patients, while a new advisory that provides previously disseminated information could be considered less urgent.

Question 3: The letter [states] that side effects of Chantix® may include "an increase in psychiatric symptoms such as anxiety, nervousness, tension, and depression as well as untoward changes in behavior." It failed to include suicidal ideation or attempted suicide. However, they were listed in the informed consent addendum that was included with the letter. Why were the most dangerous side effects omitted from the letter but included in the consent addendum?

Response: The cover letter was provided to inform study participants of the need to review the informed consent addendum, which did mention "suicidal ideation" as a side effect. The informed consent is the regulatory document of record for participants in research. Because the study participant's doctor would be the most quali-

fied professional to discuss the use of varenicline specifically with their patient, the cover letter informed the study participants that the risks of varenicline would be discussed in depth at their next study visit and that they could call study staff with concerns or questions before then. The letter also informed participants that they should contact their provider or study staff immediately if they experienced changes in behavior/mood, or if they would like to stop the medication.

The cover letter was not intended to serve as a stand-alone document that would duplicate the consent addendum, which was attached. Instead, the purpose of the cover letter was to provide a brief and concise introduction to the addendum—an addendum that explicitly listed all the potential side effects identified by the FDA's warning, including suicidal ideation and suicidal behavior.

Question 4: In retrospect, looking at the steps that were taken to notify study participants and other veterans who were taking Chantix®, should the VA have done more to confirm notification or expedite the process?

Response: VA is concerned about the time that elapsed at a number of study sites between the receipt of the letters and consent addendums by IRBs and when they were received by veterans. VA can and will be more directive to IRBs about the time in which actions and decisions are made, should the need arise again in the future. We are also concerned about the lack of follow-up by study coordinators to ensure that the IRB's directions are carried out. There is a clear need for improved follow-up in this area. The Secretary directed the Under Secretary for Health to conduct a review of the risks of medications that are likely to be used in the PTSD study population and that there has been proper notification of associated risks. ORO is to report its findings to the Secretary, and the Under Secretary for Health will provide an action plan on September 5, 2008.

Moreover, the Secretary required PBM to review VHA's medication notification system to ensure the system's policies support timely communications to patients and providers, including those in research programs. Results and an action plan were reported to the Secretary on July 29, 2008.

Question 5: *The Washington Times* reported that a VA internal report completed on March 18 found "that among 27 patients taking Chantix® who were admitted to VA hospitals for psychiatric problems since the drug was approved for the market in 2006, 11 had attempted suicide, one attempted homicide, nine had suicidal thoughts, and six were suffering from hallucinations, according to an internal report completed on March 18." Are you aware of this report? What actions did the VA take after completion of this report? Were the results of this report shared with physicians prescribing Chantix® or those involved in the smoking cessation study?

Response: VA is aware of the draft rapid cycle analysis report, dated March 18, referenced in *The Washington Times* article. This information was the preliminary product of an analysis of data gathered between September 2006 and September 2007. The varenicline analysis using the integrated database is set to run every 6 months to search for suspected severe adverse medication events of interest.

The results of the internal analysis were shared with some but not all providers. Specifically, results were shared with the Medical Advisory Panel on March 12, 2008, FDA on March 18, 2008 (by telephone) and again on April 10, 2008 (in a face-to-face meeting), the veterans integrated service network (VISN) formulary leaders, representatives from the smoking cessation technical advisory group, representatives from the mental health group and one of the principal investigators of CSP–519. Rapid cycle analyses such as this one are put in place to identify potential signals; they are not designed to determine causality, so the results are not distributed to providers across the system like drug safety warnings from FDA.

We began this analysis because the characteristics of the population within the varenicline clinical trials did not fully resemble VA's patient population, which tends to be older to experience more health problems. In October 2007, PBM and VA center for medication safety (VA MedSafe) added psychosis because of comments from field practitioners to the ICD–9 codes of interest. Specifically, VA's pharmacy benefits management group received early reports of central nervous system adverse medication events from several medical centers, which suggested the need for vigilance in our monitoring and tracking. Prior to that time, VA MedSafe was only tracking atrial fibrillation and severe dehydration, the known severe side effects associated with varenicline. The psychosis codes that were used, included specific codes for psychosis, these were not e-codes or specific codes for suicidality.

In this report, VA MedSAFE tracked the adverse medication events associated with varenicline by using and assessing VA's spontaneous adverse drug event reporting database and through administrative, integrated databases. The analysis showed,

> "a greater crude rate of severe psychosis with varenicline compared to nicotine/buproprion but do not reach statistical significance. These data show a signal for potential increased psychosis and warrant further examination to determine actual incidence and potential causality compared to control. A large number of patients receiving all of these agents (nicotine replacement, buproprion, or varenicline) have a history of psychiatric disease as identified by agents used to treat psychiatric illness or a diagnosis of psychiatric illness. This confirms our need to continue to track (the) use of varenicline and adverse medication events in our patient population as minimal data were available on the use of varenicline in this patient population upon FDA approval." [1]

The majority of the patients in the validated group (for all three cohorts) had a psychiatric history and over one half had a history of suicidal behavior.

Question 6(a): In October 2007, the Association for the Accreditation of Human Research Protection Programs (AAHRPP) conducted a site visit to the Washington, DC VA Medical Center. The Council deferred making a decision about accreditation and instead placed the medical center in Accreditation-Pending. One of the standards described as "Not Met" by AAHRPP was developing "an informed consent process and method of documentation appropriate to the type of research and the study population, emphasizing the importance of participant comprehension and voluntary participation." What is VA doing to fix the deficiencies in the informed consent process at the Washington, DC VAMC?

Response: The Washington, DC VA Medical Center (VAMC) has systematically responded to the concerns in the informed consent process identified in the October 3031, 2007 AAHRPP report. Specifically, AAHRPP noted the template document did not have investigators include the following information when appropriate: a statement that if the participant was or became pregnant, the particular treatment or procedure might involve risks to the embryo or fetus, which were currently unforeseeable, and that additional costs to the participant might result from participation in the research. They have revised their IRB policies and procedures (revised standard operating procedures were adopted June 30, 2008), developed new consent templates (which address both of the issues raised above), and revised IRB review forms. These procedures have been put in place by training IRB members, researchers, and study staff in these new procedures and in the use of the revised forms. Training has occurred through face-to-face meetings, by e-mail, and by communication of IRB findings. The Washington, DC VAMC has instituted an audit program that includes review of consent documents and observation of the consent process.

Information regarding the consent template was sent in an e-mail to principal investigators and study coordinators on July 9, 2008. An information session regarding the changes was held for principal investigators and study coordinators on Wednesday, July 30, 2008.

Question 6(b): How many other medical centers have received Accreditation-Pending from AAHRPP?

Response: Currently, 18 VA facilities, representing 26 VA facilities with Federal Wide Assurances (FWA), are in the AAHRPP accreditation-pending category. This includes the Washington, DC VAMC. The Washington, DC VAMC received a 3 year accreditation by National Committee for Quality Assurance (NCQA) in March 2005. In VA's experience, 62 percent of facilities applying for accreditation have received accreditation-pending status at the time of their first AAHRPP Council review. Thirty-eight percent received full or qualified accreditation after the first Council review.

VA leads all Federal agencies in accreditation of human research protection programs. There are a total of 115 VA facilities with FWAs to perform human research. Between December 2003 and January 2006, 59 VA facilities representing 71 VA facilities with FWAs were accredited by NCQA. NCQA contract expired in January 2006 and, under the new contract, AAHRPP has accredited 49 VA facilities representing 57 VA facilities with FWAs. This includes re-accreditation of all but 19 NCQA-accredited facilities, which have submitted AAHRPP applications and will have site visits this summer. In total, 112 out of 115 VA facilities have at least submitted applications to AAHRPP.

To date, 78 non-VA sites are listed on AAHRPP's Web site as having achieved AAHRPP accreditation.

Six VA facilities were not accredited by NCQA, and have not yet obtained AAHRPP accreditation status. Three of the six (Little Rock, Fayetteville and Lebanon) have new IRB arrangements and will apply for AAHRPP accreditation in

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[1] VA MedSafe. "Draft: National Varenicline Integrated Database and Validation Rapid Cycle Analysis Results." U.S. Department of Veterans Affairs (Internal Document).

2009. The other three have submitted their applications to AAHRPP, but have not yet been reviewed by AAHRPP's Council.

AAHRPP requires that accredited organizations meet 20 demanding standards covering five distinct domains that address the:

- Organization (the entity assuming responsibility for the human research program and applying for accreditation);
- Research review unit, including IRBs;
- Investigator;
- Sponsor; and
- Participants.

There are four actions that may be taken by AAHRPP on an application for accreditation.

Full Accreditation—An organization placed in this category meets all Standards.

Qualified Accreditation—An organization placed in this category meets almost all of the Standards. Issues requiring corrective action are minor and administrative in nature.

Accreditation-Pending—AAHRPP places an organization in this category when the organization does not meet the criteria for full or qualified accreditation, but AAHRPP considers the organization to be able and willing to take corrective actions within a reasonable time period.

Accreditation Withheld—An organization placed in this category does not meet a substantial number of accreditation Standards and the Council on Accreditation believes that the organization will not commit to undertake corrective action or otherwise be unable to meet the criteria for qualified or full accreditation in a reasonable time. There are no VA facilities in the accreditation withheld category.

Committee on Veterans' Affairs
Washington, DC
July 14, 2008

Paul Seligman, M.D., M.P.H.
Associate Director of Safety Policy and Communication
Center for Drug Evaluation and Research
Food and Drug Administration
WO51 Room 6133 HFD–001
10903 New Hampshire Ave.
Silver Spring, MD 20993

Dear Paul:

In reference to our Full Committee hearing "Why Does the VA Continue to Give a Suicide-Inducing Drug to Veterans with PTSD?" on July 9, 2008, I would appreciate it if you could answer the enclosed hearing questions by the close of business on August 20, 2008.

In an effort to reduce printing costs, the Committee on Veterans' Affairs, in cooperation with the Joint Committee on Printing, is implementing some formatting changes for materials for all full committee and subcommittee hearings. Therefore, it would be appreciated if you could provide your answers consecutively and single-spaced. In addition, please restate the question in its entirety before the answer.

Due to the delay in receiving mail, please provide your response to Debbie Smith by fax at 202–225–2034. If you have any questions, please call 202–225–9756.

Sincerely,

BOB FILNER
Chairman

U.S. Department of Health and Human Services
Food and Drug Administration
Rockville, MD.
September 16, 2008

The Honorable Bob Filner
Chairman
Committee on Veterans' Affairs
House of Representatives
Washington, D.C. 20515

Dear Mr. Chairman:

Thank you for providing the Food and Drug Administration (FDA or the Agency) the opportunity to testify at the July 9, 2008, hearing entitled "Why Does the VA Continue to Give a Suicide-Inducing Drug to Veterans with PTSD?" before the House Committee on Veterans' Affairs. Dr. Paul Seligman, M.D., M.P.H., Associate Director of Safety Policy and Communication, Center for Drug Evaluation and Research (CDER), testified for the Agency. We are responding to your letter of July 14, 2008, containing questions for the record.

We have repeated your questions below in bold, followed by our responses.

1. How many reports of suicidal ideation and attempted suicide did FDA receive priorto issuing the Early Communication?

FDA issued an Early Communication about Chantix® (varenicline) on November 20, 2007. Below is a chart containing data from FDA's Adverse Event Reporting System (AERS) for suicidal-related events for varenicline. The first column lists the "Preferred Term," describing the reported behavior. FDA arrives at the preferred term using terms described in the Medical Dictionary for Regulatory Activities (MedDRA). The second column, "Individually Reviewed Reports" spans the time period from the start of varenicline marketing, July 10, 2006, until November 27, 2007.

Reports from a "crude count" search were individually reviewed[1]and duplicates and irrelevant cases were removed. Therefore, these reports represent unique patients.

AERS DATA FOR SUICIDAL-RELATED EVENTS FOR VARENICLINE

Preferred Term	**Individually Reviewed Reports 7/10/06 to 11/27/07**
Completed suicide	18
Suicide attempt	14
Intentional self-injury	3
Self-injurious behavior	0
Suicidal behavior	0
Suicidal ideation	111
Self-injurious ideation	6
Multiple drug overdose	0
Depression suicidal	0

[1]The main utility of a spontaneous reporting system, such as AERS, is to provide signals of potential drug safety issues. Hence, when considering crude counts from AERS, it should be realized that accumulated case reports cannot be used to calculate incidence or estimates of drug risk for a particular product, as reporting of adverse events is a voluntary process and underreporting exists. Further, because of the multiple factors which influence reporting, comparisons of drug safety cannot be made from these data. Some of these factors include the length of time a drug is marketed, the market share, size and sophistication of the sales force, publicity about an adverse reaction, and regulatory actions. It also should be noted that in some cases, the reported clinical data is incomplete, and there is no certainty that the drugs caused the reported reactions. A given reaction may actually have been due to an underlying disease process or to another coincidental factor. Further, crude counts may reflect duplicates.

AERS DATA FOR SUICIDAL-RELATED EVENTS FOR VARENICLINE—Continued

Preferred Term	Individually Reviewed Reports 7/10/06 to 11/27/07
Gun shot wound	0
Intentional drug misuse	0
Overdose	1
Total number of reports	153

2. Given that Chantix® was a newly approved drug when it was included in the Smoking Cessation Study, should the VA have considered reporting both adverse events and serious adverse events?

Because this study is not being conducted under an Investigational New Drug (IND) application, and because the VA is not the New Drug Application (NDA) holder for the drug, the VA is under no obligation to report adverse events to FDA. There are no mandatory reporting requirements for this situation.

The VA clinical study involving Chantix® is a study comparing different treatment strategies for smoking cessation, some of which included drug therapy. Based on our understanding of this study, we believe that the study meets the criteria for an exemption from the IND requirements in Title 21 Code of Federal Regulations (CFR) 312.2 because:

- Chantix® is a lawfully marketed drug.
- The study is not being conducted in support of a new indication for use for Chantix® or to support any other significant change in labeling.
- The study is not intended to support a significant change in the advertising for Chantix®.
- The study does not involve a route of administration or dosage level or use in a patient population or other factor that significantly increases the risks (or decreases the acceptability of the risks) associated with the use of Chantix®.
- It is our understanding that the study is being conducted in compliance with the requirements for institutional review set forth in 21 CFR Part 56 and with the requirements for informed consent set forth in 21 CFR Part 50.
- It is our understanding that the study is being conducted in compliance with 21 CFR 312.7, regarding promotion and charging for investigational drugs.

3. The VA did not change the reporting requirements to include both Adverse Events (AEs) and Serious Adverse Events (SAEs) until after the February 1 warning. Should the VA have changed its policy after the Early Communication?

The reporting requirements for adverse events observed in clinical trials are established in 21 CFR 312.32 for studies that are conducted under an IND. This study does not require an IND; hence, the study sponsor (the VA) and the Institutional Review Board (IRB) are responsible for determining what reporting should be employed for the study. This responsibility reflects their familiarity with the trial design and the ethics of the study in the particular patient population being studied.

4. In your opinion should the Early Communication have prompted the VA to modify the protocol given the unique population of the study?

The VA, as the sponsor of the study, is responsible for overseeing this trial, including obtaining the informed consent of study subjects and making sure new information is provided to study subjects (where appropriate), with oversight by the IRB. This local application of the regulations guiding research is appropriate and essential. For instance, 21 CFR 50.25 describes the basic elements of informed consent, listing eight basic elements, each of which requires some interpretation. The second element states that the following information shall be provided to each subject in a study: "A description of any reasonably foreseeable risks or discomforts to the subject." What is "reasonably foreseeable" is a matter of judgment, including important insights that the study sponsor and the IRB can bring to bear about the ethics of a study in a specific population. With this in mind, for preliminary communications of emerging safety issues, the study sponsor and the IRB must play a critical role in determining whether or not a given study protocol or informed consent procedures or information, would need to be modified as new safety information was made available to them.

In the Early Communication about Chantix®, FDA stated that it had received, and was evaluating, reports of neuropsychiatric symptoms in patients who had taken Chantix®, but had not reached a conclusion about whether this information warranted regulatory action. The Early Communication did not draw any conclusions regarding a causal relationship between Chantix® and these symptoms. It was appropriately within the discretion of the study sponsor, with oversight by the IRB, to determine whether the information contained in the Early Communication required modification of the informed consent procedures or information for study subjects or changes to the study protocol.

5. How many reports of AEs or SAEs has the FDA received from the VA?

A search of the AERS database revealed 10 adverse event reports from various VA facilities from the time the drug was marketed, July 10, 2006, to June 19, 2008. One case reported an outcome of death, but the available information did not cite a suicide. Not all reporters who submit AERS reports indicate which institution or facility they are reporting from. Therefore, it is possible that the number of cases being reported from the VA may not be fully represented.

6. What action should physicians take when the FDA issues an Early Communications or Public Health Advisories for a drug?

Early Communications are issued to keep healthcare professionals and the general public informed of postmarked safety issues that are currently being evaluated by FDA. Early Communications are issued at the beginning of FDA's assessment, prior to conclusive determination of the clinical or public health significance of the information under evaluation, and before a decision has been made about what regulatory actions, if any, should be taken. They reflect FDA's current analysis of available data concerning these drugs, but posting the information as an Early Communication does not mean that FDA has concluded a causal relationship between the drug and the emerging safety issues. It also does not mean that FDA is advising healthcare professionals to discontinue prescribing these products. The intent of an Early Communication is to inform healthcare professionals and patients about how best to use a marketed drug, so that they can make individual decisions.

Public Health Advisories are issued to provide information regarding important public health issues to the general public, including patients and healthcare professionals. For example, Public Health Advisories may highlight an emerging drug safety issue, announce the implementation of methods to manage the risks identified for a marketed drug, or provide other important public health information. Public Health Advisories regularly include recommendations to mitigate a potential risk and often are issued in conjunction with other drug safety communications, such as Healthcare Professional Sheets. However, selection of specific drug products or treatment regimens for particular patients are decisions to be made between the patient and physician familiar with the individual's current health status and past medical history. These decisions are considered the practice of medicine and are not regulated by FDA.

7. What is the requirement for Black Box warnings?

Certain contraindications or serious warnings, particularly those that may lead to death or serious injury, may be required by FDA to be presented in a box. According to 21 CFR 201.57(c)(1), a boxed warning ordinarily must be based on clinical data, but serious animal toxicity may also be the basis of a boxed warning in the absence of clinical data. A boxed warning is ordinarily used to highlight for prescribers one of the following situations:

- There is an adverse reaction so serious in proportion to the potential benefit from the drug (e.g., a fatal, life-threatening or permanently disabling adverse reaction) that it is essential it be considered in assessing the risks and benefits of using a drug.
- There is a serious adverse reaction that can be prevented or reduced in frequency or severity by appropriate use of the drug (e.g., patient selection, careful monitoring, avoiding certain concomitant therapy, addition of another drug or managing patients in a specific manner, avoiding use in a specific clinical situation).
- FDA approved the drug with restrictions to assure safe use because it concluded that the drug can be safely used only if distribution or use is restricted (e.g., under 21 CFR Part 314, Subpart H, § 314.520, "Approval with restrictions to assure safe use").

A boxed warning can also be used in other situations to highlight warning information that is especially important to the prescriber. Information included in the WARNINGS AND PRECAUTIONS and CONTRAINDICATIONS sections should

therefore be evaluated to determine whether it should also be placed in a boxed warning.

Boxed warnings are more likely to be based on observed adverse reactions, but there are instances when a boxed warning based on an expected adverse reaction would be appropriate. For example, a contraindication during pregnancy, based on evidence in humans that drugs in a pharmacologic class pose a serious risk of developmental toxicity during that time, would usually be in a boxed warning for all drugs in that class, even those in which the adverse reaction has not been seen.

A boxed warning can also be considered for a drug that has important risk/benefit information that is unique among drugs in a drug class (e.g., to note that a drug is the only one in its class to have a particular risk that makes it inappropriate for use as a first line therapy).

8. Is the FDA considering a Black Box warning for Chantix®?

FDA is still reviewing data, and a decision regarding the addition of a boxed warning has not yet been made.

Thank you again for the opportunity to testify. Please let us know if you have any further questions or concerns.

Sincerely,

Stephen R. Mason
Acting Assistant Commissioner for Legislation

Committee on Veterans' Affairs
Washington, DC.
July 14, 2008

Ponni Subbiah, M.D., M.P.H.
Vice President, Medical Affairs
Pfizer Inc.
325 7th Street, NW, Suite 1200
Washington, DC 20004

Dear Ponni:

In reference to our Full Committee hearing "Why Does the VA Continue to Give a Suicide-Inducing Drug to Veterans with PTSD?" on July 9, 2008, I would appreciate it if you could answer the enclosed hearing questions by the close of business on August 20, 2008.

In an effort to reduce printing costs, the Committee on Veterans' Affairs, in cooperation with the Joint Committee on Printing, is implementing some formatting changes for materials for all full committee and subcommittee hearings. Therefore, it would be appreciated if you could provide your answers consecutively and single-spaced. In addition, please restate the question in its entirety before the answer.

Due to the delay in receiving mail, please provide your response to Debbie Smith by fax at 202–225–2034. If you have any questions, please call 202–225–9756.

Sincerely,

BOB FILNER
Chairman

Pfizer Inc.
Corporate Affairs
Washington, DC.
August 20, 2008

VIA FACSIMILE AND EMAIL

ATTN: Ms. Debbie Smith

The Honorable Bob Filner
Chairman
Committee on Veterans' Affairs
U.S. House of Representatives
335 Cannon House Office Building
Washington, D.C. 20515–6115

Dear Chairman Filner:

The enclosed attachment ("Attachment 1") is submitted on behalf of Dr. Ponni Subbiah, in response to your letter, dated July 14, 2008, requesting that Dr. Subbiah provide follow-up answers to your hearing questions for the hearing record.

In addition, Pfizer Inc ("Pfizer") respectfully submits that the attached records (PFIZER–CVA–000000001 through 000000003) contain or constitute confidential and proprietary information of Pfizer provided to the Committee pursuant to your requests for such information as Chairman of the Committee on Veterans' Affairs ("Committee"). Accordingly, Pfizer has marked all records produced today with the legend "PFIZER CONFIDENTIAL TREATMENT REQUESTED."

We respectfully request that the Committee afford these records the maximum protection available to information provided to the Committee. Pfizer respectfully requests that the Committee, your staff, and all those who may review Pfizer records on behalf of the Committee protect against the disclosure of this confidential and proprietary information. The intentional or inadvertent disclosure of information that Pfizer has expressly designated as confidential and proprietary may cause substantial harm to Pfizer. We also respectfully request advance notice of any contemplated disclosure of Pfizer's confidential and proprietary information, and a reasonable opportunity to object. Please direct any such notice to me directly.

If you have any questions, or need additional information, please do not hesitate to call me at (202) 783–7070.

Sincerely,

Dolly Judge
Vice President, Government Relations

cc: Hon. Steve Buyer, Ranking Member
Committee on Veterans' Affairs

ATTACHMENT 1

1. You said that [the] clinical trial program for Chantix® involved more than 5,000 patients over a 10-year period. Did any of those patients have PTSD or underlying psychiatric illnesses?

- The development program for Chantix® involved more than 5,000 patients over a span of 10 years.
- Patients who disclosed that they were receiving treatment for (or had a history of) serious psychiatric illnesses such as schizophrenia, bipolar disorder, and depression did not participate in the pre-approval clinical trial program for Chantix®.
- Pfizer has not conducted a study of the use of Chantix® in patients with PTSD.

2. How many reports of suicidal ideation and attempted suicide did Pfizer receive prior to the FDA issuing the Early Communication?

- FDA Early Communication was issued on November 20, 2007.
- Prior to the FDA releasing an early communication regarding Chantix®, Pfizer received the following numbers of post-marketing suicide-related adverse event reports (worldwide) through November 19, 2007:
  - Reports of Suicidal ideation—322
  - Reports of Suicide attempt/Suicidal behavior—37
  - Reports of Completed suicide—16
- Based on estimated global exposure, approximately 5.2 million patients had been prescribed Chantix® through November 2007.
- According to the Centers for Disease Control, there are 11 completed suicides per 100,000 persons per year in the United States.[1]
- According to surveys conducted by Harvard Medical School, between 2.8–3.3 percent of U.S. residents aged 15–54 years have had suicidal ideation in a 12-month period.[2]
- According to a German epidemiology study, a smoker is 2.6 times more likely to commit suicide than a non-smoker.[3]

3. Do you think this drug is appropriate for use for veterans with PTSD?

- Pfizer cannot make a judgment in the abstract whether a particular medication is appropriate for a particular patient.
- We can say that the smoking rate in PTSD patients has been reported to be up to 60 percent and 48 percent of combat veterans with PTSD are also heavy smokers (≥25 cigarettes per day).[4–5]
- It is important to note that patients with psychiatric illnesses such as PTSD also may have other comorbidities that can lead to serious health consequences. Due to the high rate of smoking in patients with PTSD and therefore higher risk of smoking-related comorbidities such as cardiovascular disease, cancer,

and lung diseases, it is important to continue to improve the standard of medical care and provide treatment options for PTSD patients to quit smoking.[6]

- Smoking cessation, with or without treatment, is associated with nicotine withdrawal symptoms and has also been associated with the exacerbation of underlying psychiatric illness.[7–9]
- Whether a medication is appropriate for a particular patient is a decision that can be made only by that patient's doctor, after consultation with the patient. When considering the use of Chantix® for their patients, healthcare providers should discuss the risks of smoking, the health benefits of quitting smoking, and the product's efficacy and safety profile, including the potential for psychiatric symptom exacerbation. Symptoms experienced in prior quit attempts, with or without Chantix®, should also be discussed. Health care practitioners managing patients with concurrent psychiatric disorders who are quitting smoking should take this information into consideration when advising their patients.

4. In your testimony you state that the report of an adverse event does not necessarily mean there is a causal relationship between the product and the event. Are there a certain number of adverse events, of maybe a certain nature, that have to be reported to establish a causal relationship?

a. What would have to happen to establish a causal relationship?

- Causality assessment relies on the medical and scientific review of the totality of available evidence rather than purely on the number of events.
- The information needed to assess causality comes from multiple sources including randomized controlled clinical trials, and observational studies. Post-marketing reports, preclinical mechanistic experiments, and individual case reports may generate hypotheses to test in clinical trials and observational studies but typically cannot establish causation.
- It is important to understand the nature of spontaneous adverse event reporting. These reports can come from any person or source ranging from consumers to healthcare providers, and from phone calls to Internet postings. Often these reports lack sufficient medical information to enable meaningful assessment of causality. As a result of this variability in reporting, any analysis of the numbers of adverse events should be considered hypothesis-generating only, and should be considered within the overall context of an existing body of scientific and public health knowledge. Despite the limitations of adverse event reporting, Pfizer actively follows up on adverse event reports to obtain as much information as possible.
- In the case of Chantix®, a causal relationship between these post-marketing reports and the use of Chantix® has not been established. However, in some reports related to Chantix®, a causal relationship could not be excluded.

5. Please provide to the Committee a list of all the paid Pfizer consultants to VA along with their salaries.

- The type of information requested is not typically available in the payment systems and databases kept by Pfizer. We do not maintain a single database for all payments to consultants. Further, our databases do not provide the granularity of detail requested, i.e., the relationship of a consultant to the VA. We have used our best efforts to be as accurate and responsive as possible. Therefore, our response today is based on Pfizer's current information and belief.
- In the records submitted to the Committee, we have included a list of individuals paid by Pfizer, including, but not limited to, clinical investigators, speakers, or individuals paid for teaching, writing, or other consulting services ("Consultants"), who have a known affiliation with a VA medical center or institution. The speaker Consultants payment information covers all Pfizer products spanning the period of January 1, 2007 to the present. (see PFIZER-CVA-000000001 thru 000000003). In summary, Pfizer made payments to 68 Consultants totaling approximately $895,000.
- Pfizer sponsors a variety of research conducted by outside healthcare providers to research Pfizer medicines. To ensure compliance with various laws and industry standards, all forms of research activities, including those related to clinical trials, should have genuine scientific value, include investigators selected on the basis of criteria relevant to the research effort, and involve compensation consistent with the value of the research actually provided. In most instances, Pfizer contracts with a full service Contract Research Organization (CRO) to manage study sites and investigators.

- Pfizer typically makes the clinical trial payments to the CRO, who then pays the investigator or institution pursuant to the agreement between the CRO and the investigator or institution. Therefore, it is difficult to track payments at the individual investigator level for Pfizer-sponsored research related payments made to CROs. However, the information provided to the Committee represents our best effort to identify all Pfizer-sponsored clinical protocols in which the Consultants listed participated as an investigator.
- With regard to our speaker programs and other consulting services, Pfizer requires all speaker Consultants to sign an agreement under which the Consultant represents and warrants that he/she has the full power and authority to enter into the agreement. The agreement also requires that the consultant will perform all services and preparation activities in accordance with all applicable laws, regulations, and other criminal and civil legal requirements and in compliance with relevant Pfizer's policies on speaking consultants.

6. How much money has Pfizer invested in the development, testing, and marketing of Chantix®?

- At this time, Pfizer is unable to provide a reasonable cost associated with the development, testing, and marketing of Chantix®.
- The information requested is not typically available in the databases kept by Pfizer. Calculating the total cost for any single drug would be extremely burdensome and challenging. Any attempt to estimate a total cost within any valuable degree of precision would have to rely upon numerous factors, complex calculations, multiple assumptions, and involve highly confidential and proprietary data. Pfizer believes that the figure would likely be in the hundreds of millions of dollars. In fact, the Pharmaceutical Research and Manufacturers of America estimates that discovering, developing, and obtaining FDA approval of a new prescription drug, on average, takes between 10–15 years and costs between $800 million and $1 billion dollars.[10]

7. How much money does Pfizer stand to lose if Chantix® were pulled from the market?

- Pfizer respectfully disagrees with the premise of the question. Pfizer cannot reasonably speculate about the inestimable costs and lost revenues associated with withdrawal of a product from the market.
- Based on all the data currently available including clinical trials, epidemiology, post-marketing reports, as well as on the collective professional opinion of Pfizer's Medical team, Pfizer continues to believe that the benefits of Chantix® outweigh the risks and that this important medicine is appropriately labeled for both healthcare professionals and patients.

[The attachment to the letter will be retained in the Committee files due to confidential personal information included in the attachment.]

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Committee on Veterans' Affairs
Washington, DC
July 14, 2008

John D. Daigh, Jr., M.D., CPA
Assistant Inspector General for Healthcare Inspections
Office of the Inspector General
U.S. Department of Veterans Affairs
Washington, DC 20420

Dear John:

In reference to our Full Committee hearing "Why Does the VA Continue to Give a Suicide-Inducing Drug to Veterans with PTSD?" on July 9, 2008, I would appreciate it if you could answer the enclosed hearing questions by the close of business on August 20, 2008.

In an effort to reduce printing costs, the Committee on Veterans' Affairs, in cooperation with the Joint Committee on Printing, is implementing some formatting changes for materials for all full committee and subcommittee hearings. Therefore, it would be appreciated if you could provide your answers consecutively and single-spaced. In addition, please restate the question in its entirety before the answer.

Due to the delay in receiving mail, please provide your response to Debbie Smith by fax at 202–225–2034. If you have any questions, please call 202–225–9756.

Sincerely,

BOB FILNER
Chairman

U.S. Department of Veterans Affairs
Washington, DC.
August 22, 2008

The Honorable Bob Filner
Chairman
Committee on Veterans' Affairs
United States House of Representatives
Washington, D.C. 20515

Dear Mr. Chairman:

This is in response to your July 14, 2008, letter to Dr. John Daigh, Assistant Inspector General for Healthcare Inspections, Office of Inspector General, following the July 9, 2008, hearing on "Why Does the VA Continue to Give a Suicide-Inducing Drug to Veterans with PTSD?" Enclosed are Dr. Daigh's answers to the additional hearing questions.

Thank you for your interest in the Department of Veterans Affairs.

Sincerely,

GEORGE J. OPFER
Inspector General

Enclosure

Questions from the Honorable Bob Filner
For John D. Daigh, Jr., M.D., CPA
Assistant Inspector General for Healthcare Inspections
Office of Inspector General U.S. Department of Veterans Affairs
Before the Committee on Veterans' Affairs Hearing
"Why Does the VA Continue to Give a
Suicide-Inducing Drug to Veterans with PTSD?"

Question 1: In your testimony, you state that the revised consent form was only given to patients that entered the study after April 9, 2007, and that individuals who had signed the original second consent form were not re-consented during the research study. Is this normal procedure? Even if the known risks at the time were

changes in dreams and nausea, shouldn't study participants have been re-consented?

Response: There are four Informed Consent Documents referred to in the written statement:

- The first Informed Consent Document (screening ICD) was a screening form, which, if the veteran qualified, was signed to bring the veteran into the study.
- The second ICD (original second consent form) detailed the risks and benefits of participating in the treatment and identified possible smoking cessation drugs that could be used in the study. Chantix® was not one of the drugs listed in the second ICD.
- The third ICD (revised consent), approved by the Washington, DC, VA Medical Center Institutional Review Board (IRB) in April 2007, identified the option of using Chantix® as one of the study drugs and listed the side effects as nausea and changes in dreams.
- The fourth ICD (addendum), approved by the IRB in February 2008, was an addendum to the second and third ICDs, which listed the more serious side effects of Chantix®, suicidal ideation, and erratic behavior.

The Veterans Health Administration (VHA) Handbook 1200.5 requires that all patients be advised of new risks that might affect their willingness to participate further in the study. The IRB had approved a revised consent form in April 2007 and then approved an addendum in March 2008. All 15 patients enrolled in the study who were taking Chantix® should have been informed of the new risks twice and given the opportunity to withdraw from the study or continue by signing the revised ICD in April 2007 and again in March 2008.

Question 2: Given that the Smoking Cessation Study included Chantix® during the post-market monitoring period should site investigators have reported all adverse events along with serious adverse events?

Response: The Food and Drug Administration and the VHA Handbook requires investigators to report serious adverse events not all adverse events.

Question 3: You said in your testimony that "the facility's research service did not ensure that patients involved in the smoking cessation study were notified of the risk of suicidal thoughts or behavior in a timely manner." What do you consider timely?

Question 3(a): Do you think patients should have been notified of the risk after the Early Communication?

Response: VHA Handbook 1200.5 states that "significant new findings developed during the course of the research which may relate to the subject's willingness to continue participation will be provided to the subject." We do not have an opinion on whether the early communication was considered a significant new finding.

Question 3(b): Should the patients have been notified by phone rather than by mail?

Response: The principal investigator was responsible for ensuring that notification occurred. Whether that notification is accomplished by telephone, mail, or other method is not as pertinent as the lack of follow up action to verify that study participants ever received the notice. After the beginning of our review, a number of patients came in person to the medical center to sign the fourth ICD. We did not consider this to be timely notification of the risks associated with Chantix®.

Question 3(c): Whose responsibility is it to ensure the patients are notified.

Response: It is part of the principal investigator's responsibility and the IRB's responsibility to determine if the information is a significant new finding. If the IRB and the principal investigator decide that new findings warrant notifying the study participants, they need to take steps to ensure that the information reaches the study participants.

Question 4: Did the Site Investigator, any member of the IRB, or study coordinator explain why they failed to list the most dangerous side effects in the letter?

Response: The Palo Alto Cooperative Studies Program Coordinating Center explained that there was a desire not to unduly alarm participants.

Question 5: If there were so many issues with this study at the VAMC DC, how do we know that the other sites involved in this study do not have similar problems?

Response: Due to time limitations, we focused on the Washington, DC, VAMC and we did not review other sites. The Secretary directed the Office of Research Oversight to review the other sites.

Committee on Veterans' Affairs
Washington, DC
July 14, 2008

Gerald P. Koocher, Ph.D., ABPP
Dean and Professor
School of Health Sciences
Simmons College
300 The Fenway
Boston, MA 02115

Dear Gerald:

In reference to our Full Committee hearing "Why Does the VA Continue to Give a Suicide-Inducing Drug to Veterans with PTSD?" on July 9, 2008, I would appreciate it if you could answer the enclosed hearing questions by the close of business on August 20, 2008.

In an effort to reduce printing costs, the Committee on Veterans' Affairs, in cooperation with the Joint Committee on Printing, is implementing some formatting changes for materials for all full committee and Subcommittee hearings. Therefore, it would be appreciated if you could provide your answers consecutively and single-spaced. In addition, please restate the question in its entirety before the answer.

Due to the delay in receiving mail, please provide your response to Debbie Smith by fax at 202–225–2034. If you have any questions, please call 202–225–9756.

Sincerely,

BOB FILNER
Chairman

Questions from the Honorable Bob Filner
for Gerald P. Koocher, Ph.D.
Professor and Dean, School of Health Sciences, Simmons College
Before the Committee on Veterans' Affairs Hearing
"Why Does the VA Continue to Give a
Suicide-Inducing Drug to Veterans with PTSD?"
July 9, 2008

Question 1: In your testimony you highlight that obtaining consent does involve documentation, but is best conceptualized as a process by which the investigator makes certain that potential participants know what will be asked of them, what risks or hazards may be involved, what benefits may result. What is your professional opinion of the fact that the VA OIG could not find documentation regarding informed consent of the patient in the research trial that was being done and when there was a change, i.e. Chantix®, that there was no documentation regarding re-consenting?

Response: I described consent as a process because offering a document for signature does not necessarily imply that the people participating in the study understand what they have been asked to sign. Not everyone can or does read and understand a written form fully. The conversation between the research team and participants forms a critical communication bridge.

- If the VA OIG reported that it could not find documentation regarding consent of participants in a research trial I and/or when a change in protocol occurred, I would want to ask several questions:
- Where did the OIG look (e.g., in patients' medical records, in the investigators' research files at each site, in the minutes or IRB meetings, etc.)?
- What did the investigators at each site report regarding the notation of consent and storage of that notation?
- How did the investigators at each site explain the missing documentation?
- Did the OIG inquire of the IRB officials at each site about the IRB monitoring, auditing, and recordkeeping for all research protocols; and if so, did the IRB officials behave differently in the case of this particular study.
- When were IRBs asked to approve the introduction of Chantix® to the research protocol, and how long did it take each IRB to approve the revised protocols and consent forms?
- After such protocol changes occurred, what did the IRB require the site investigators to do by way of notification and what deadlines were specified?

- Because the studies in question involved multiple sites, was a DSMB in place? If so, what do the DSMB minutes reflect about any required notifications, or changes in procedure? If no DSMB was in place, why not?

By listing these questions I hope to underscore the complexity of your question. I cannot reach a conclusion about the adequacy of the VA OIG investigation or the thoroughness of the standard protections that one would expect to find at each clinical site (i.e., local IRBs or an over-arching DSMB). I simply have no basis to reach any conclusion about who "dropped the ball" or even whether "the ball was dropped."

My understanding some of the testimony before the Committee suggested that some physicians may have prescribed Chantix® to individual patients who also happened to be enrolled as study participants. In such circumstances the prescribing of that medication could fall beyond the scope of the study (i.e., the investigators may not have had no way of knowing that some of their research participants had been prescribed the drug by physicians not associated with the study). Three types of protections might have prevented such problems:

- Most studies involving vulnerable populations have "rule out" requirements that would disqualify some type of vulnerable people from participating (e.g., people on certain medications or with certain pre-existing medical or mental conditions that would contraindicate participation). You may wish to determine whether the research project had such criteria.
- In studies that run for many months investigators typically ask patients if their medical condition has changed in any way during return visits. You may wish to ascertain whether such questions were part of the research protocol. Of course, this step will only prove useful if research participants remember and report any such changes.
- Private physicians writing a prescription for Chantix® would normally ask patients what other medications and treatments they were receiving. If a patient informed their personal physician about research participation and treatment for PTSD, I would expect such a physician to investigate the protocol or speak with the investigators before initiating a new drug regimen that might potentially interact adversely with the protocol. You may want explore whether those physicians who prescribed Chantix® made such inquiries.

Question 2: Do you believe that common sense and good judgment should be exercised by the researchers? In the instance where there was no followup ensuring that patients had been informed, who and how would you hold the participating parties responsible?

Response: Standard practice in any research involving people as participants demands that the investigators seek institutional approval, through their IRB: 1) of any research protocol and consent forms/processes prior to beginning data collection; and 2) on any changes in the research protocol or consent form. In addition, investigators must notify their IRBs and any over-arching DSMBs of all adverse incidences. The investigators should retain copies of all such notifications. IRBs and DSMBs must keep minutes that reflect their deliberations and actions. One would expect such minutes to include notification dates or instructions, action steps, and monitoring plans, if any.

If an investigator failed to notify an IRB/DSMB of protocol changes, consent form changes, or adverse events, I would be inclined to hold the investigator responsible. I suspect his/her IRB would do so as well.

If an IRB or DSMB failed to address such changes or notifications in a timely manner, I would be inclined to hold the respective Boards' administrators responsible.

The key problem in the study of concern to the Committee is a determination of who had relevant information regarding protocol changes, who passed on that information, who received that information, what actions did they take based on the information available to them, and whether they were acting in a reasonable timeframe.

I have no data on which to form an opinion on these points in the case at hand.

I hope you find these comments to your questions responsive and helpful.

Sincerely,

Gerald P. Koocher, Ph.D., ABPP

Committee on Veterans Affairs
Washington, DC.
July 29, 2008

The Honorable James B. Peake, M.D.
Secretary
U.S. Department of Veterans Affairs
810 Vermont Avenue, NW
The Fenway
Washington, DC 20240

Dear Secretary Peake:

Thank you again for your testimony at the U.S. House of Representatives Committee on Veterans' Affairs hearing that took place on July 9, 2008, on "Why Does the VA Continue to Give a Suicide-Inducing Drug to Veterans with PTSD?"

As Chairman of the Committee, I formally request a list of the 64 patients who were given the smoking-cessation drug Chantix® by the Department of Veterans Affairs (VA) and who have not signed an addendum to the informed consent form that the VA had given to Chantix® users. These 64 patients were mentioned in your testimony at the hearing.

Thank you again for taking the time to answer this request. The Committee looks forward to receiving your answers by August 29, 2008.

Sincerely,

BOB FILNER
Chairman

The Secretary of Veterans Affairs
Washington, DC.
September 26, 2008

The Honorable Bob Filner
Chairman
Committee on Veterans' Affairs
U.S. House of Representatives
Washington, DC 20515

Dear Mr. Chairman:

This is in response to your letters formally requesting a list of patients given the smoking-cessation drug Chantix® and who were mentioned in my testimony at the Committee's July 9, 2008, hearing. I regret the delay in this reply.

The Department of Veterans Affairs (VA) is providing the Committee with the signature pages of the informed consent addendums of 91 of the 120 veteran patients participating in the smoking-cessation study who were known to receive Chantix® after February 1, 2008. The patients' names and the witness' names are withheld to protect patient privacy. We are also providing documentation of notification for the 27 other participants who have not yet signed an informed consent addendum. These individuals have been notified of the potential side effects of Chantix® by their physician or a member of the research staff, or have received a copy of the consent addendum (documented by FedEx or United States Postal Service receipt). These records have also been redacted to ensure patient confidentiality. Two patients are no longer participating in the study. All patients currently participating in the study and receiving Chantix® since February 1, 2008, have signed the addendum or received information about the Food and Drug Administration warning.

At the time of the hearing, there were 64 veterans who were known to receive Chantix® after February 1, 2008, who had not signed the addendum to the informed consent. Thirty-five of these patients have now signed consent addendums, either as a result of these contacts or in the course of a routine study visit. These 35 are included in the 91 signature pages we have provided.

The patients' names are redacted because the researcher had obtained a Certificate of Confidentiality (enclosed) from the Department of Health and Human Services for the smoking cessation study. Under title 42, United States Code, §241 (d)), the signed Certificate of Confidentiality protects the researcher from being compelled to release the names or identifying characteristics of any research subject in any Federal, State, or local civil, criminal, administrative, legislative, or other proceedings. Section 241 (d) protects the privacy of human subjects who participate in research for the betterment of science and medicine.

Individuals participate as subjects in research because they know the Certificate of Confidentiality protects their identities. The release of identities could have a chilling effect on voluntary participation in research, particularly in the area of mental health.

Sincerely yours,

James B. Peake, M.D.

Enclosures

[The attachments to the letter will be retained in the Committee files due to confidential personal information included in attachment.]